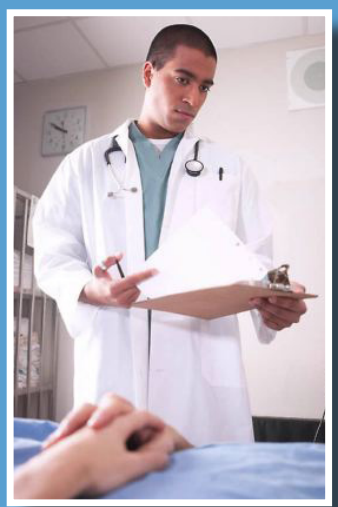

PECARN PRIMER

EMSC Emergency Medical Services for Children NATIONAL RESOURCE CENTER

Revised Edition

A Guide for Research Coordinators in the Pediatric Emergency Care Applied Research Network

Cite As:

Haymon, Jaclynn; Kim, Emily; Goldfarb, Sherry; Shreve, Kate; Jacobson, Kammy, Wagner, Duke; Jones, Grant; McDuffie, Rachel; Thomas, Bobbe; and Zuspan, Sally Jo (editor/designer: Suzanne Sellman). PECARN Primer: A Guide for Research Coordinators in the Pediatric Emergency Care Applied Research Network (Revised Edition). Washington, DC: Emergency Medical Services for Children (EMSC) National Resource Center (NRC). July 2013.

The EMSC NRC, located just outside Washington, DC, was established in 1991 to help improve the pediatric emergency care infrastructure throughout all 50 states, the District of Columbia, and the five U.S. territories. The EMSC NRC is housed within Children's National Medical Center, one of America's leading pediatric institutions serving sick and injured children and their families. In 2012, the EMSC NRC received its fifth (multi-year) funding award to provide support to the federal EMSC Program.

The federal EMSC Program is designed to ensure that all children and adolescents – no matter where they live, attend school, or travel – receive appropriate care in a health emergency. It is administered by the U.S. Department of Health and Human Services' Health Resources and Services Administration, Maternal and Child Health Bureau. To date, the federal EMSC Program has provided grant funding to all 50 states, the District of Columbia, five U.S. territories, and the free associated states of Micronesia, Palau, and the Marshall Islands.

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PECARN
Pediatric Emergency Care Applied Research Network

Funding for the EMSC NRC is provided by the Health Resources and Services Administration, Maternal and Child Health Bureau, Emergency Medical Services for Children Program through grant number U07MC09174."

EMSC
Emergency Medical Services for Children
NATIONAL RESOURCE CENTER

Welcome to PECARN

The Emergency Medical Services for Children (EMSC) National Resource Center (NRC) welcomes all research coordinators (RC) and research assistants (RA) to the Pediatric Emergency Care Applied Research Network (PECARN). RCs are a vital part of PECARN – they are responsible for enrolling patients, completing paperwork, entering data, and working with hospital staff to make PECARN studies happen. The purpose of this toolkit is to orient RCs to the EMSC Program, PECARN, and their role within PECARN. The toolkit is divided into the following four sections: Brief History of EMSC and PECARN, Introduction to Research and Resources for the Researcher, Setting Up and Running a PECARN Study, and PECARN's Internal Communication Structure. Use this toolkit to learn how to navigate eRoom, use PECARN data systems, prepare for a site monitoring visit, recruit and retain patients, and much more.

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SECTION I:
A BRIEF HISTORY OF EMSC AND PECARN

Chapter 1 About the EMSC Program

Emergency Medical Services for Children (EMSC) is the only federal program that focuses on improving the pediatric components of emergency care. The EMSC Program, within the Health Resources and Services Administration's (HRSA) Maternal and Child Health Bureau (MCHB), was first authorized by U.S. Congress in 1984. In fiscal year 1985, the EMSC Program received its first federal appropriation in the amount of $2 million. Almost three decades later, the appropriation has grown to approximately $21 million. The EMSC Program was conceived as national initiatives designed to improve emergency medical services (EMS) and emergency department (ED) care for children aged 0 to 21.

The overall goals of the EMSC Program are to ensure access to state-of-the-art emergency medical care, including primary prevention, prehospital care, emergency care, acute care, and rehabilitation for children and adolescents. Program goals include improving existing EMS systems and developing and evaluating improved procedures and protocols for treating children. To date, federal appropriations have allowed the Program to assist all 50 states, the District of Columbia, and five U.S. territories (American Samoa, the Commonwealth of the Northern Mariana Islands, Guam, Puerto Rico, the U.S. Virgin Islands and the Freely Associate States (the Federated States of Micronesia Palau and Marshall Islands)) in achieving these goals. Academic medical centers have also contributed significantly toward achieving EMSC goals, both through grants and cooperative agreements.

Overview of EMSC Funding Mechanisms

The EMSC Program provides funding to states to support developments in an EMS system infrastructure to provide appropriate pediatric emergency care. To include professional education and training to improve the clinical care of children, standardizing equipment guidelines, and developing tools for medical assessment of critically ill and injured children. In later years, the guidance documents focused on additional areas that emerged as important to EMSC or to MCHB as a whole, such as caring for children with special health care needs, enhancing the ability to provide family-centered care, cultural competence, regionalization of pediatric care, economic analysis, and other areas identified in the Program's five-year strategic plans.

Brief History of EMSC Grants, Contracts, and Cooperative Agreements

Prior to 1997, state system development grants, known as "Demonstration" grants, enabled all states to begin addressing their EMS systems' challenges in caring for children. Their intent was to encourage grantees to explore strategies that could improve the system of emergency care for children. Once many of these strategies had been developed, various "Implementation" grants were provided to encourage newly funded states to implement these strategies. In 1998, the "State Partnership" grant was developed to support states and territories in ongoing efforts to improve children's emergency services. These grants are primarily used to sustain EMSC improvements and to continue integration of pediatric emergency care within the state's EMS system of care. Examples of this integration may include formalized pediatric protocols or regulations, state legislation or regulations that create a permanent EMSC coordinator position, a permanent pediatric representative on a state's EMS Board, or improvements to data collection for EMSC.

"Targeted Issue" grants were first funded by the Program in 1991 and are meant to address specific needs or concerns that transcend state boundaries. Typically, the projects result in a new product or resource, or the demonstration of the effectiveness of a model system component or service considered to be "of value to the nation."

"Special Grant Initiatives" are used to focus on particular areas of concern to the EMSC Program. These consisted largely of research grants co-funded with MCHB's Research Program or other Department of Health and Human Services (DHHS) agencies, such as the Agency for Healthcare Research and Quality (AHRQ), the Centers for Disease Control and Prevention (CDC), and the National Institute of Mental Health (NIMH). As of FY 1991, Special Grant Initiatives have included:

- The Native American Project for Alaska and Hawaii; FY 1991
- Enhancing Pediatric Patient Safety; FY 2001
- The Network Development Demonstration Project; FY 2001
- Clinical Practice Guidelines; FY 2002
- National Trauma Registry for Children Planning Grants; FY 2003
- State Partnership Regionalization of Care (SPROC); FY 2012

The SPROC grant program is the most recent funding to address a key recommendation of the Institute of Medicine's report "Hospital Based Emergency Care: At the Breaking Point" to support pediatric regionalization of care demonstration projects. The purpose of each demonstration project is to "reach beyond state borders to overcome barriers to specialized pediatric medical and trauma services." For more information about SPROC grants go to the EMSC website at: http://www.emscnrc.org/Grantee_Portal/SPROC.aspx.

Resource and data management centers are a critical part of the EMSC Program. They enhance the ability to manage and provide resources, guidance, and consultation to all EMSC grantees in the 50 states, five territories, and the District of Columbia. Funded as two cooperative agreements, these centers are currently the EMSC National Resource Center (NRC) and the Data Coordinating Center (DCC), which houses the National EMSC Data and Analysis Resource Center (NEDARC). The EMSC NRC provides guidance to EMSC grantees and works closely with national professional organizations to: disseminate and implement best practices in pediatric emergency care, identify resources and model programs; develop interfacility transfer guidelines/agreements; and develop legislation and regulations. The DCC has two major functions: to help grantees and state EMS offices develop their own capabilities to collect, analyze, and utilize EMS and other healthcare data to improve the quality of care in state EMS and trauma systems; and to serve as the data coordinating center for the Pediatric Emergency Care Applied Research Network (PECARN).

EMSC Program Support

Since 1985, the EMSC Program has funded more than 400 new grants, contracts, and cooperative agreements focusing on pediatric emergency care issues. The Program has also conducted or sponsored workshops, national conferences, training sessions, working meetings, and webcasts.
Recently, performance measures (a set of requirements that State Partnership grantees are working towards as part of their grant requirement) have become a critical priority for all HRSA grantees, particularly for MCHB and EMSC grantees. The EMSC Program provides substantial consultation and resource development to help State Partnership grantees develop and meet these measures. Specifically, the EMSC NRC and NEDARC have each devoted an entire section of their websites to the measures. In addition, the EMSC NRC and NEDARC have conducted webcasts, published detailed manuals and guides, and offered tailored workshops and training sessions.

The Program and its resource centers have also collected and disseminated numerous EMSC products and supported research-related activities. For more on the EMSC Program, visit the EMSC NRC website at http://www.emscnrc.org or the NEDARC website at http://www.nedarc.org.

Chapter 2 About PECARN

PECARN is the first federally-funded, multi-institutional network for research in pediatric emergency medicine in the United States. Its goal is to conduct meaningful and rigorous multi-institutional research into the prevention and management of acute illnesses and injuries in children and youth across the continuum of emergency medicine health care.

PECARN works with diverse demographic populations and across varied geographical regions to promote the health of children in all phases of care. To accomplish these tasks, PECARN provides the leadership and infrastructure needed to promote multi-center studies, supports research collaboration among EMSC investigators, and encourages informational exchanges between EMSC investigators and providers.

PECARN Organizational Structure

In 2001 (and again in 2005, 2008, and 2011), the EMSC Program awarded cooperative agreements to academic medical centers through a competitive mechanism known as the EMSC Network Development Demonstration Project (NDDP). In September 2002 (and again in 2006 and 2012), a cooperative agreement was awarded to the University of Utah to serve as the Data Coordinating Center (DCC) for PECARN. In 2012, the NDDP expanded from four cooperative agreements to six. Each NDDP grant recipient is referred to as a Research Node Center (RNC).

A year later, in 2013, an EMS Resource Node Center (E-RNC) was added. The purpose of this demonstration project is to test the feasibility of conducting effective multi-institutional pediatric prehospital research.

Each RNC collaborates with two other Hospital Emergency Department Affiliates (HEDAs) representing academic, community, urban, general, and children's hospitals. The E-RNC collaborates with two additional Emergency Medical Services Affiliates (EMSAs). Together, each RNC/E-RNC and its collaborating HEDAs/EMSAs make up a "node" in PECARN. With 21 HEDAs/EMSAs total, the PECARN network serves more than 1.2 million acutely ill and injured children every year. For more information about PECARN, visit its website at www.pecarn.org.

Each RNC/E-RNC works collaboratively with its HEDAs/EMSAs to develop and submit nodal research proposals to PECARN and conduct PECARN-approved research at their respective institutions. The seven nodes are:

CHaMP	Charlotte, Houston, and Milwaukee Prehospital EMS Research Node Milwaukee County EMS, Mecklenburg EMS Agency, Houston Fire Department EMS
GLEMSCRN	Great Lakes Emergency Medical Services for Children Research Network University of Michigan, Children's Hospital of Michigan, Nationwide Children's Hospital
HOMERUN	Hospitals of the Midwest Emergency Research Node Cincinnati Children's Hospital Medical Center, Washington University School of Medicine, Children's Hospital of Wisconsin-Medical College of Wisconsin
PEM-NEWS	Pediatric Emergency Medicine Northeast, West and South Children's Hospital of New York, Texas Children's Hospital, Children's Hospital of Colorado
PRIDENET	Pittsburgh, Rhode Island, Delaware Network Children's Hospital of Pittsburgh, Hasboro Children's Hospital, Al Dupont Hospital for Children
PRIME	Pediatric Research in Injuries and Medical Emergencies University of California-Davis, Children's Hospital of Philadelphia, Primary Children's University of Utah
WBCARN	Washington, Boston, Chicago Applied Research Node Children's National Medical Center, Children's Hospital of Boston, Children's Memorial Hospital

Data Coordinating Center

The DCC provides network leadership and coordination within the following areas:

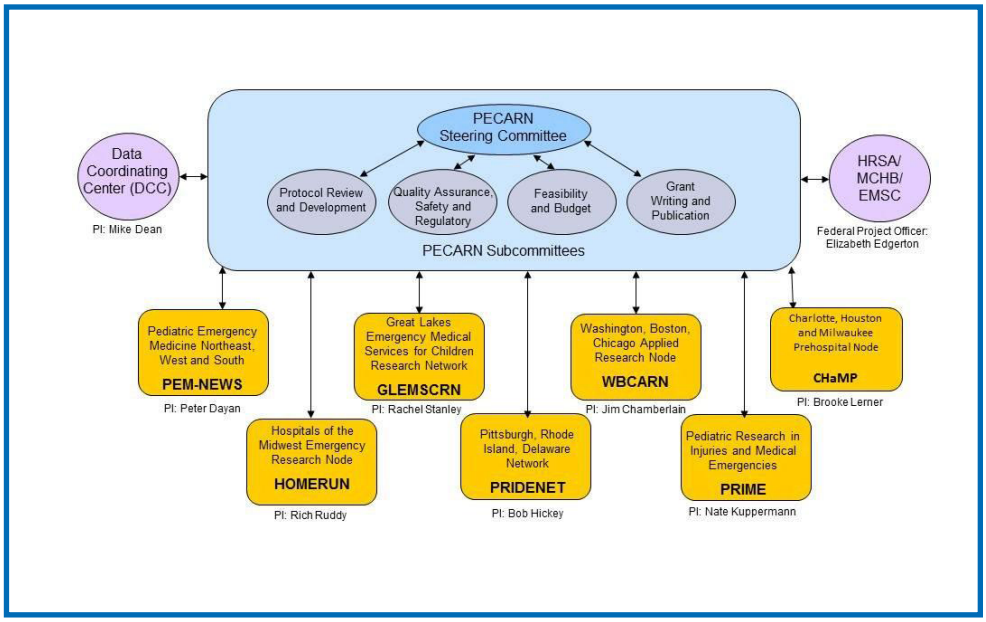
- network/site organization;
- protocol development/study design;
- grant writing;
- subcommittee participation;
- training/education;
- manual and study material development;
- study support and technical expertise;
- data management; and
- data analysis.

The DCC is the central repository for most study information. This information is made available to PECARN through eRoom (see Section III – eRoom Monitoring). The DCC is required to centrally track most study regulatory documents from both PECARN and non-PECARN sites participating in PECARN research studies. The DCC staff members are an excellent resource for RCs, their team, and the entire PECARN.

PECARN Steering Committee and Subcommittees

PECARN is governed by a Steering Committee comprised of 19 voting members: three members from each node and one from the DCC. The Steering Committee formulates and monitors policies and procedures guiding all research activities and provides comprehensive scientific review and approval for all research proposals. All major scientific and operational decisions are made by majority vote of the Steering Committee (see Diagram 1). Four subcommittees have been created to carry out specific tasks identified by the Steering Committee: Protocol Review and Development; Quality Assurance, Safety, and Regulatory; Feasibility and Budget; and Grant Writing and Publication.

Diagram 1



PECARN Staff Structure

The personnel structure for each node is as follows:

- nodal principal investigator (nodal PI): responsible for nodal leadership
- nodal administrator (NA) or nodal manager (NM): responsible for overseeing PECARN study implementation at nodal HEDAs
- HEDA principal investigator (HEDA PI): responsible for overseeing implementation of all PECARN studies at the HEDA
- study site principal investigator (study site PI): responsible for a specific PECARN study at the HEDA site
- site RC: managing day-to-day PECARN research activities at the site

PECARN Review Process

In PECARN, each node works collaboratively with other nodes and with HRSA's MCHB to develop and implement network research. All new research concepts must be approved by a nodal PI to begin the PECARN review process. The PECARN Steering Committee must formally approve concepts and research protocols before an investigator (internal or external) can

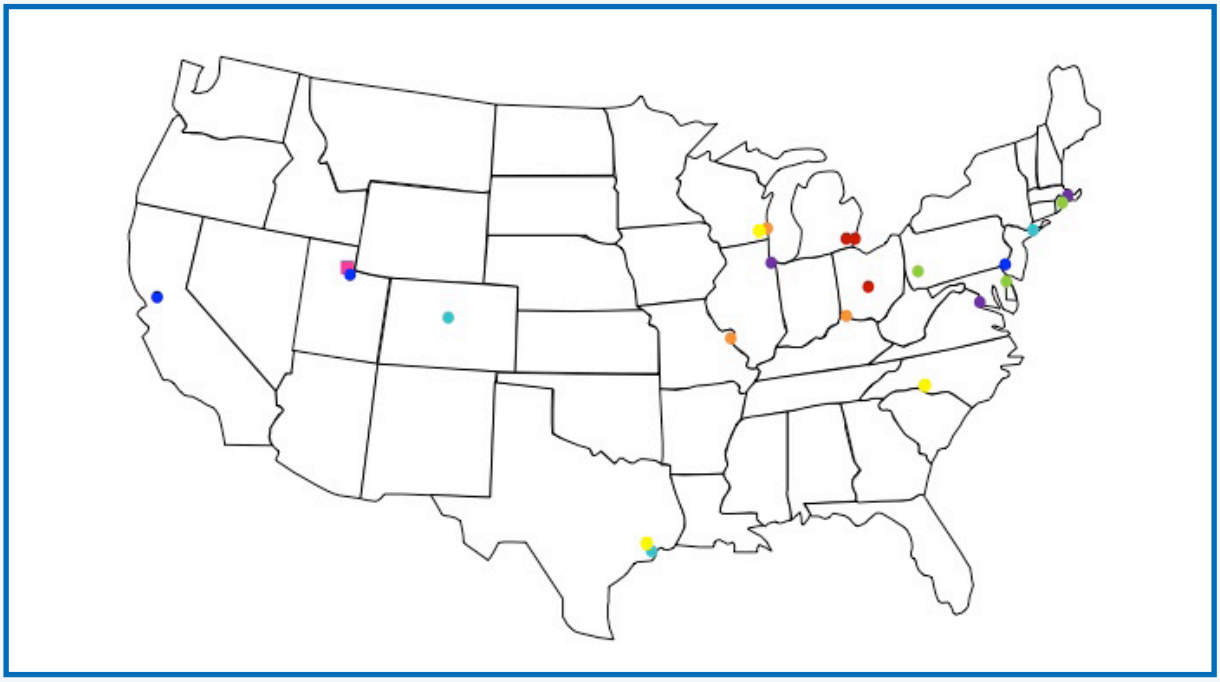
write up his/her study proposal to submit as a grant application using the resources or the name of PECARN. (Most research projects require extramural research funding to be conducted through PECARN). To better understand the PECARN review process, visit the PECARN Training website.

PECARN Policies

All PECARN standard operating procedures (SOPs) can be accessed in eRoom (see Section III – eRoom Monitoring). PECARN policies guide network operations that affect each HEDA. RCs should become familiar with PECARN policies, especially those that directly govern HEDA research activities. It is also important to know where the policies and procedures are located in case of an audit.

Activity 1: Map the HEDAs

Using the map, name the HEDAs for each node.



Node	HEDAs/EMSAs

Activity 2: Describe SOPs

Describe the importance of having SOPs for the network.

SECTION II:
INTRODUCTION TO RESEARCH AND RESOURCES FOR THE RESEARCHER

Chapter 3 Research Design

Domains of Research

Research comes in many forms – bench, clinical, and health services to name a few (see Table 1). For more information about research and study designs, refer to the resources listed in Section V – Research Resources.

Table 1: Research Domains

Bench Research	Clinical Research	Health Services Research
• The first phase of any research study. • Typically involves studies on cells, tissues, or animals. • Refers to other types of research that may use human blood or tissue but is not conducted in live human beings.	• Research that involves observation or intervention with human subjects. • Typically occurs after a bench research study to develop a drug or intervention and involves human subjects as opposed to animals.	• Research that involves a study of health systems, how care is delivered, access to care, costs associated with care, or other systems issues.

Study Designs

Human subjects are used for studies in several ways. Two common study types used in PECARN are observational and interventional. Observational studies observe behavior or collect data without changing the course of care that a patient gets or changing anything about the patient. By contrast, interventional studies are those where there is a specific change that the investigator makes to the course of care a patient receives; for example, administering a drug for research purposes. Observational and interventional studies can be designed in several different ways. Table 2 includes definitions of commonly used study designs.

Table 2: Commonly Used Study Designs

Type of Study	Advantages	Disadvantages
Cohort: These observational studies are widely used to determine the incidence or risk factors associated with a condition or disease. A cohort is a group of people who share the same characteristics or experiences.	Safe, subjects can be matched, can establish timing and directionality of events, eligibility criteria and outcome assessments can be standardized, easier and cheaper to administer than randomized controlled trials (RCT).	Controls may be difficult to identify, exposure may be linked to a hidden confounder, blinding is difficult, randomization not present, and, for a rare disease, large sample sizes or long follow-up is necessary.[1]

Type of Study	Advantages	Disadvantages
Case Control: Also known as retrospective studies, case control studies compares a group of patients with a specific disease or outcome to another group of patients without the disease or outcome. The goal is to determine the relationship between the risk factor and the disease through retrospective review. This is an observational study because no intervention is taken to alter the disease or outcome. Study Design 101 by Himmelfarb Health Sciences Library. George Washington University http://www.gwumc.edu/library/tutorials/studydesign101/index.html	Enables the researcher to study rare health outcomes. It is also quicker, cheaper, and easier than conducting a cohort study. This is because researchers know that the patients have a health outcome of interest and are looking back at the factors that affected that health outcome rather than waiting for the health outcome to occur.	Greater chance of having bias in the study because the health status of the patient is known before the researcher determines the contributing factors. There can be bias in interpretation, as well as the limitation of having existing data that may or may not have captured the exposures of interest.
Cross-Sectional: This type of study is generally used to determine prevalence and/or causation. Prevalence describes the number of cases in a population during a period of time. Knowing the prevalence of a particular disease aids the investigator to determine the predictive value or likelihood of a particular diagnosis. Reference: Observational Research Methods. Research Design II: Cohort, cross sectional, and case control studies. C J Mann. *Emergency Medical Journal* 2003; 20: 1 54-60. Retrieved from http://emj.bmj.com/citmgr?gca=emermed;20/1/54 .	Fast and inexpensive, commonly referred to as "snap-shot" studies. They are considered "ethically safe."[2] Cross-sectional studies are useful for generating hypotheses.	Establishes association at most, not causality because it is only looking at one point in time. It is susceptible to recall bias and the confounders may be unequally distributed. Also the group sizes may be unequal.

In addition to observational and interventional studies, other common study types include:

Ecological Studies. Ecological studies compare characteristics of populations resulting in incidence and prevalence measures. They are usually easy to conduct but can result in an "ecological fallacy." The ecological fallacy is an error in the interpretation of statistical data, whereby inferences about the nature of individuals are based solely upon aggregate statistics collected for the group to which those individuals belong. This fallacy assumes that all members of a group exhibit characteristics of the group at large.

Randomized Controlled Trial. This is a clinical trial in which patients are randomly assigned to receive one of several clinical interventions or to a control group; the assignments are based on chance alone. One of these interventions is the standard of comparison or control. The control may be a standard practice, a placebo ("sugar pill"), or no intervention at all. Someone who takes part in a RCT is called a participant or subject. RCTs seek to measure and compare the outcomes after

the participants receive the interventions. Because the outcomes are measured, RCTs are quantitative studies and can be conducted in the following ways:

- ***Open Trial.*** The researcher and participant both know about what treatment they are receiving. This is done in situations, such as studying a surgical technique, where it would be unethical to treat the participant without their full knowledge or it is impossible to hide the intervention.

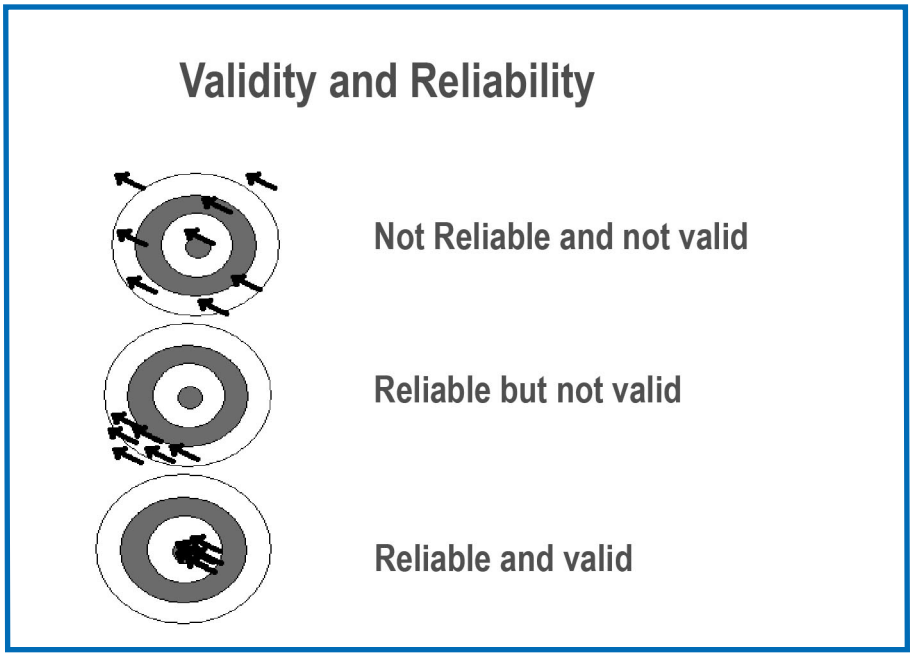
- ***Single-Blinded Trial.*** The researcher knows the details about the treatment but the participant does not know what treatment, interventional, standard, or placebo, he/she is receiving. This is done when the participant is responsible for reporting health outcomes to reduce bias from their interpretation.

- ***Double-Blinded Trial.*** The treatments used in the study are coded so the researcher administering the treatment and the participant do not know which one was used.

- ***Triple-Blinded Trial.*** Similar to a double-blinded trial but a third party, such as a statistician or assistant researcher or a radiologist reading the film, also does not know which treatment was used. This is commonly done in double-blinded trials and therefore the term triple-blinded trial is rarely used.

Diagram 2

Reliability and Validity in Research



Reliability is the extent to which an experiment, test, or any measuring procedure yields the same result on repeated trials. Without the agreement of independent observers replicating research procedures, or the ability to use research tools and procedures that yield consistent measurements, researchers would be unable to satisfactorily draw conclusions, formulate theories, or make claims about the generalizability of their research.

Validity refers to the degree to which a study accurately reflects or assesses the specific concept that the researcher is attempting to measure. While reliability is concerned with the accuracy of the actual measuring instrument or procedure, validity is concerned with the study's success at measuring what the researchers set out to measure.

Researchers should be concerned with both external and internal validity (see Diagram 2). External validity refers to the extent to which the results of a study are generalizable or transferable. Most discussions of external validity focus solely on generalizability (see Campbell and Stanley, 1966.[3)] Internal validity refers to (1) the rigor with which the study was conducted (e.g., the study's design, the care taken to conduct measurements, and decisions concerning what was and wasn't measured) and (2) the extent to which the designers of a study have taken into account alternative explanations for any causal relationships they explore (see Huitt, 1998[4]). In studies that do not explore causal relationships, only the first of these definitions should be considered when assessing internal validity.

For any research to be accurate, it needs to be both reliable and valid. Reliability in a clinical research study is measured by how consistent the results are. In other words, how many times can the experiment be repeated and get a similar result? The more similar the result, the more reliable it is; however, this does not mean the results are valid. Validity occurs if some-

thing "represents accurately those features of the phenomena that it is intended to describe, explain, or theorize."[5] In a valid study, the researcher is obtaining results that accurately depict the true values of the measured value, while reliability simply measures how many times a researcher gets the same result…not necessarily the correct one.

Research Bias and Cofounding Variables

The two major threats to a study's validity are research bias and confounding variables.

Research Bias. In the context of a research study, the concept of "bias" refers to "a systematic departure from the true results, affecting the reliability and validity of a study." In other words, bias occurs when the implementation of the study affects the outcome of the study. Therefore, a study should be designed to eliminate or at least reduce bias. Two common types of bias are reviewer and exposure. A brief description of each is provided below.

- Reviewer bias is when the researcher "collecting or reviewing data (either subjective or objective) is inappropriately blinded or is aware of a suspected diagnosis or results of a reference test."[6]
    - ***How it happens.*** When a researcher wants to test a new drug and the researcher knows what drug the participant received, his interpretation of whether or not the participant improved might be affected.
    - ***How to control it.*** This type of bias is prevented by conducting a double-blinded study (neither party knows what drug was used, the test drug or standard care/placebo).
- Exposure bias occurs while assigning each participant to a treatment group.
    - ***How it happens.*** This bias occurs when there is no protocol for assigning participants to a treatment, allowing a researcher to decide whether to assign a participant to the treatment or control group. This allows for the possibility that the researcher could assign people to a group based on how he thinks a participant will perform in the study.
    - ***How to control it.*** To avoid these biases, researchers use the process of randomization to assign participants to a treatment or control group, which assures an equal chance of being assigned to either group. Maintaining randomization is important because it ensures that there are no characteristics of assignment that will cause a bias. For example, suppose participants are being enrolled in a large clinical trial where they are randomly assigned to Drug A or Drug B. Randomization is done such that each site gets an equally distributed number of participants in each drug group.

Ensuring Randomization in PECARN Studies

Although there are different methods for randomly assigning participants, a telephone system is one method that has been used for PECARN studies. The telephone randomization system internally keeps track of the assignments so each of the 19 sites has a balanced enrollment (recall that each site is to have an equal distribution of Drug A and Drug B). If someone forgets to call the randomization system and instead picks up the next vial, which happened to be Drug A, he/she would therefore be assigning the participant to a group on their own. This is a protocol violation and can adversely affect the clinical study if, due to non-random selection, more participants at a site received Drug A than Drug B.

Two events that increase bias are loss of follow up and self-selection.

- ***Loss to Follow Up.*** Loss to follow up occurs when participants cannot be reached for follow-up tests or follow-up interviews. This bias is one of the most common uncontrolled biases; many participants either forget about the study, are too busy to call the researcher, or move away and forget to update their contact information.

- ***Self-Selection.*** This is when participants volunteer themselves to participate in a study, or when they refuse to participate in a study. "Volunteers may be more health conscious or even healthier than the general population, and this may favorably affect the efficacy of the screening study. It is difficult to predict and quantify differences between a volunteer and target population, and randomization is considered to be an effective tool to address this type of bias."[7]

The more bias in a study, the less reliable and valid it is. While real world factors make it impossible to have a perfectly bias-free study, it is the researcher's responsibility to do everything (ethically) under his/her control to eliminate bias. Randomization and blinded studies are techniques that help eliminate bias.

Confounding. During a research study, independent variables which are not typically studied in a clinical trial, (e.g., population, hospital culture, legislation, or media awareness), but nevertheless may affect the study's outcomes, are referred to as confounders.[8] Confounding is a mixing of effects, which can make it look like there is a relationship between two variables when actually, there is none. Alternatively, a true relationship may be masked by confounding. Human behavior and outcomes are complex, and there are numerous mechanisms that can affect outcomes.

- ***How it happens.*** Suppose researchers want to compare the hospital outcomes of those who received medication in the prehospital setting to those who did not. Findings show that the outcomes for those who did not receive medication were actually better than the outcomes for those who did. However, this does not take into account that those who received medication were likely to have a more severe illness in the first place. This situation is referred to as confounding.

- ***How to control it.*** Researchers can eliminate, or at least reduce, sources of bias and confounding by carefully designing the data project or study. For more information on bias and confounding sources and possible solutions, see "Overcoming Sources of Bias & Confounding" available on the NEDARC website at www.nedarc.org.

The importance of a multi-center research network, such as PECARN, is that it addresses many of the issues discussed above and captures sufficient cases to conduct powerful and meaningful studies. Since children are basically healthy, it is difficult to enroll large numbers of children with a particular condition at an individual site. By pooling the HEDA participant populations together, PECARN is able to obtain a sample of sufficient size to be able to adequately study a particular condition, disease, or intervention.

Activity 3: Research Design

Talk with a PECARN investigator or RC about the different research designs and the design of current PECARN studies. Hint: A current listing and description of the study is available on the PECARN website (http://www.pecarn.org) under "Current Research."

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[7]http://radiology.rsnajnls.org/cgi/content/full/238/3/780
[8]This discussion of confounding is based on the resources provided by the National EMSC Data Analysis Resource Center at http://www.nedarc.org.

Chapter 4 Research Ethics

During the last 50 years, the ethical conduct of research has received increasing attention, especially with the creation of Institutional Review Boards or IRBs (see Section II – Institutional Review Boards). Most people equate ethics with the distinction between right and wrong. However, another way to define ethics is as a "method, procedure, or perspective for deciding how to act and for analyzing complex problems and issues."[1]

In PECARN, both medical ethics and ethical conduct of research is considered. RCs should be familiar with the ethical principles which guide the conduct of research. If at any time an RC feels that there is an ethical conflict, contact the supervisor, PI, nodal administrator, or the DCC to discuss the issue. For example, an RC hears an enroller state "you should enroll in this study because this drug is probably the best way to help your child." If the purpose of the study is to determine the effect of the drug, then this statement is not truthful and, therefore, not ethical.

Below is a list of principles which guide the ethical conduct of research.

- Autonomy: Independent actions and choices of research participants should not be constrained.
- Non-maleficence: A duty not to inflict harm.
- Beneficence: A duty to help others and do what is best for them.
- Telling the truth: A responsibility to disclose all pertinent information.
- Professional responsibility: An obligation to observe the rights, rules, and principles of medical/research ethics.
- Informed consent: "A process of communication between a participant and physician that results in the participant's authorization or agreement to undergo a specific medical intervention."[2]
- Confidentiality: An implicit promise that divulged information will not be revealed.
- Distributive justice: A responsibility to distribute benefits and burdens equally and to allocate scarce resources fairly.

Activity 4: Ethical Conduct of Research

Pick one of the above principles of ethical conduct of research and describe its importance to PECARN, using one current study as an example. A current list of PECARN studies can be found on the PECARN website (www.pecarn.org) under "Current Research."

References

[1] Resnik, David B. "What is Ethics in Research and Why is it Important?" National Institute of Environmental Health Sciences, http://dir.niehs.nih.gov/ethics/whatisethics.htm accessed 8/1/2007

[2] AMA, Informed Consent, http://www.ama-assn.org/ama/pub/category/4608.html accessed 8/1/2007

Chapter 5 Good Clinical Practices

Good Clinical Practices (GCP) is the term that refers to all regulations and guidelines that set minimum standards for proper conduct of clinical trials. They are designed to (1) ensure the quality and integrity of data obtained from clinical testing and (2) protect the rights and welfare of clinical subjects.

Investigators, and all research staff, conducting human subjects research are responsible for ensuring the safety and rights of participants in studies. This includes ensuring that all protocol administration processes are properly documented so that any audit or monitoring of the study clearly demonstrates protocol and regulatory compliance.

In accordance with GCP, the investigator is obligated to:

- obtain and maintain appropriate training to assume responsibility for proper conduct of the trial;
- maintain a list of properly qualified persons to whom the investigator has delegated duties;
- ensure that all persons assisting with the study are adequately trained with respect to the protocol and investigational procedures or products, and that their duties documenting these trainings to the study are recorded in the Essential Documents Binder (EDB);
- ensure that protocols conform to ethical and scientific standards and that the study is conducted according to the protocol (see Protocol Violations sidebar);
- ensure that the process for obtaining consent is done in an ethical manner within regulatory standards and properly documented; and
- ensure that the study protocol administration is properly and consistently documented with clear, legible notes, including who wrote the note on what date.

Protocol Violations

A protocol violation occurs when the way something is done varies from how it is described in the study protocol. A protocol deviation is described as an intentional choice which is not protocol compliant. Regardless of what happens, violations must be reported to the DCC as described for the study. The DCC usually has a form or method to report all protocol violations and deviations. Protocol violations do not mean the site is doing a bad job. Early reporting of a violation will help the DCC teach other sites how to avoid the violation. Early reporting will also notify the DCC that the data could be affected by the violation. It is important for the study team to keep good detailed notes on the events and circumstances surrounding the violation. Most sites' IRBs allow the reporting of minor protocol violations at the time of continuing review.

The textbook reference to GCP has historically been about how error corrections in the chart and/or research record should be made to provide clarity to the integrity of the data.

For more information on GCP, visit the Food and Drug Administration's (FDA) Office of Good Clinical Practice website at http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/OfficeofScienceandHealthCoordination/ucm2018191.htm. Additionally, there are numerous published works from the Clinical Trials industry that summarize and explore the details of current best practices in research documentation to be compliant with all relevant regulations.

Training in GCP

To ensure that investigators and research staff are informed about GCP, most institutions require the completion of training courses. Research training requirements vary from one HEDA to the next. Consult the HEDA PI for information on each institution's research training requirements. Many sites require the satisfactory completion of Collaborative Institutional

Training Initiative (CITI) Responsible Conduct in Research Curriculum (see www.citiprogram.org/rcrpage.asp). In addition, many IRBs will require investigators to fulfill good clinical practices training requirements in the form of a class or online test. Contact the local IRB for more information.

The PI and key personnel must complete training in research with human subjects as required by the Office of Human Research Protections (OHRP) (see Section II – Research Regulations and Oversight). The agency operates under the Code of Federal Regulations (CFR) Title 45 part 46. This code covers information on IRBs, requirements for consent, and considerations for children in research. For more information, visit the HHS Code of Federal Regulations (see www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html) and NIAID Human Subjects Certifications and Training (see www.niaid.nih.gov/researchfunding/sop/pages/hstraining.aspx).

American Health Insurance Portability and Accountability Act of 1996

Along with GCP, PECARN researchers must adhere to regulations set forth by the American Health Insurance Portability and Accountability Act (HIPAA). The main goals of HIPAA are to improve the healthcare system by making medical records available online and to protect information within medical records by creating and enforcing standards. To read more about HIPAA and the security and privacy rules within the Act, visit HHS Health Information Privacy (see www.hhs.gov/ocr/privacy/hipaa/understanding/index.html).

Be mindful when working with electronic records. Many devices now, especially USB port storage drives, make it very easy to obtain data. Increasingly, these portable devices are required to have encryption when being used for research data. Also, email is not a secure form of communication. Be sure to follow the site's policy for computer use and data storage.

Chapter 6 Fraud in Clinical Research

Surprisingly, many serious incidents of fraud in clinical research surface across the country each year. While the most famous cases seem unbelievable and egregious, there are many more cases of less serious acts or errors that constitute fraud and result in serious consequences. It is the responsibility of all research staff to be aware of errors in research that could constitute fraud or have some perception of fraud.

Many incidents of possible fraud are more likely simple errors or omissions. However, if audited, even simple mistakes or omissions can lead to exclusion of a site's data from the final analysis or a citation by a federal agency. For this reason, it is important to keep all data clean and to follow all regulations. Report all protocol deviations to ensure honesty about study errors that have occurred. For all other issues that come up, document specific situations in a note to file (see Note to File sidebar).

Note to File

A note to file is any written documentation or note that includes information that cannot be recorded elsewhere. There is no standard document for a note to file; each site may design a document or simply record the information on a piece of paper. If a note to file documents a mistake or protocol violation made in the course of the study, an explanation of the event along with a plan of action to ensure that it doesn't happen again is required. As with any document, the note to file needs to be signed and dated by appropriate personnel and reference the subject (if applicable) and protocol.

What is Fraud?

The FDA defines fraud as "falsification of data in proposing, designing, performing, recording, supervising, or reviewing research or in reporting research results. Falsification includes both acts of omission (consciously not revealing all data) and commission (consciously altering or fabricating data)."

Fraud does not include honest error or honest differences of opinion. Deliberate or repeated noncompliance with the protocol and GCP can be considered fraud, but it is considered secondary to falsification of data.[1]

According to a survey of 3,000 NIH-funded scientists (published in the June 9, 2005, issue of Nature) "1 in 3 NIH-funded scientists confesses to having sinned." Approximately 12% admitted to looking the other way when colleagues used flawed data.

Remember, it is often simple errors, omissions, or even "well-intended" commissions that get a site into trouble. So what types of problems could raise concern about a site's performance?

- backdating of forms
- documents dated by others
- losing consent forms
- any data reported to the data center that cannot be substantiated by source documents
- missing documents
- falsifying follow up calls
- complaints by participants
- erroneous dates on assessments or labs
- consents initialed by study coordinator instead of participant
- many consent forms dated by someone else other than the participants
- inaccurate medical histories that make it appear that the participant doesn't meet inclusion criteria

- all participants compliant with study medication
- no significant adverse events (SAE) reported when it is expected that they exist (e.g. a life threatening event or event that led to hospitalization or disability)
- no subjects lost to follow up
- lack of source documentation to support study entry criteria

If any of these items come up, don't panic. Some of these events can be related to simple errors or may simply represent reality. These types of events do not usually result in serious consequences, but they could create an appearance of fraud at the site. In cases in which something like this is happening at a site, a note to file can be of great value. The IRB may also need to be informed (see Section II – Institutional Review Boards).

Examples of Fraud

Example 1. While reviewing a data form, the RC notices a missing respiratory rate on a child in the study. The ED physician says that she remembers this participant and the respiratory rate was 32. The coordinator documents this on the data collection form (it is allowed to be a retrospective field). Later the RC realizes that there is no source for this data point; the physician never wrote the value in the chart. Now the RC has just documented a data point for which there is no source document. Simply document the situation in a note to file, inform the PI, and don't do it again.

Example 2. What if the PI, trying to be diligent and complete, reviewed consent forms and initialed his signature every time he noted a blank signature that was supposed to be for the participant's initials? The PI was not trying to commit fraud, but rather thought he was just dutifully filling in blanks. What should be done to correct the situation? Notify the physician that this was incorrect, have the physician write a note to file, and contact the IRB. The IRB may want participants to initial the consent forms correctly.

Be aware of what can raise red flags in a research study. Conduct things "by the book;" know the regulations and comply with them. If an error is made, write a note to file and document everything that happened. Contact the IRB as appropriate. RCs can always contact the DCC for advice.

For more information about fraud, read "RA Rights & Responsibilities" by Rachel McDuffie, MPH (GLEMSCRN). The article was published in Spring 2007 issue of *PECARN In a Nutshell* (see www.pecarn.org/media/pdfs/PECARN_Newsletter_Spring2007.pdf).

Activity 5: Is It Fraud?

Determine if the action described constitutes fraud.

1. A patient's vitals were taken 30 minutes late; the values were recorded for the time they were taken.
2. Data is entered from memory, there is no written record.
3. A patient came into the clinic a day after enrollment stopped, and data analysis is scheduled to start next week. The RC enrolls the patient by backdating the forms.

References

[1]Source: Scientific Misconduct-the "F word" Woolen, S and Hage, A, October 2001

Chapter 7 Research Regulations and Oversight

RCs play an important role in research regulatory compliance. While the primary responsibility for research with human subjects is vested in the PI conducting a study, others engaged in the conduct of the research, such as the research staff, share this responsibility. This includes responsibility to comply with the laws, regulations, and institutional policies that regulate research. The two federal agencies that oversee the conduct of research are OHRP and the FDA.

Office of Human Research Protections

OHRP establishes criteria for and approves assurances of compliance for the protection of human subjects with institutions engaged in human subject research conducted or supported by DHHS. PECARN is funded under DHHS and therefore federal regulations (CFR Title 45 part 46) apply to PECARN research activities.

OHRP provides clarification and guidance to research institutions, develops educational programs and materials, and promotes innovative approaches to enhancing human subject protections. They also can audit a site for compliance with federal regulations. Access the OHRP website (see www.hhs.gov/ohrp/) and look under the regulations section for important information governing the conduct of human subjects research. Every RC and PI should be familiar with these regulations.

OHRP has three divisions that directly ensure criteria for compliance are followed and that assist institutions with their research.

- **Compliance**. The Compliance division evaluates all written substantive allegations or indications of noncompliance with DHHS regulations. The relevant institution is notified of the allegation and is asked to investigate the basis for the complaint. The institution then provides a written report of their investigation, along with relevant IRB and research records, to OHRP who determines what, if any, regulatory action needs to be taken. This is one of several federal agencies that can come to the institution to do an audit of research practices.
- **Education**. The Education division conducts national and regional conferences, and develops and distributes materials to improve protections for human subjects in research. Quality improvement consultations are also available for institutions to assess and improve their human subjects research protection programs.
- **Policy and Assurances**. This division prepares policy and guidance documents. They also interpret the requirements for human subject research and administer the assurance of compliance.

For questions about these regulations, contact the NA or the DCC. RCs should always discuss basic compliance issues with PECARN leaders rather than calling OHRP directly.

The Food and Drug Administration

The FDA's main purpose is to guarantee safety in the nation's food, medicine, make-up products, and other products that affect health. The FDA also tries to create innovative medicines and technologies that assure greater safety of food and

medicine. To guarantee maximum safety of food, cosmetics, medicine, and biological products, the FDA creates standards for any product intended for human and animal consumption.

Code of Federal Regulation (CFR) 21 gives the FDA the power to regulate food and drugs in the United States. To make a new drug available to the public, it must first be submitted to the FDA for approval. The Center for Drug Evaluation Research (CDER), which operates under the FDA, is involved throughout the clinical trial process; even in the design of the research studies. The CDER ensures that patients in research studies are not harmed or unnecessarily put in danger. CFR section 21 "contains most of the regulations pertaining to food and drugs. The regulations document all actions of all drug sponsors that are required under Federal law."[1] "Part 312 of section 21 covers investigational new drug application regulations, including regulations for clinical investigators."[1] The FDA can also grant exemption from informed consent which is covered later in this chapter.

In general, FDA regulations are applicable to PECARN when a node is studying a drug or device. However, the EMSC Program expects all PECARN research studies to be conducted according to the most stringent FDA regulations. This helps to ensure that PECARN is prepared for the conduct of studies regulated by the FDA.

For more information on Part 312 of section 21, visit: http://www.fda.gov/cder/about/smallbiz/CFR.htm.

Note that PECARN research is conducted under the International Conference on Harmonization's (ICH) Good Clinical Practice Guidelines, The International Standard of Research Conduct. The GCP guidelines describe the role of the sponsor and the investigator in clinical trials. For more information about ICH, visit: http://www.ich.org/LOB/media/MEDIA482.pdf.

References

[1]Federal Regulations for Clinical Investigators, (www.fda.gov/cder/about/smallbiz/CFR.htm), accessed 8/6/2007

Chapter 8 Institutional Review Boards

An Institutional Review Board (IRB) is a committee established at hospitals, universities, and other research institutions to protect the rights and welfare of the participants and families who participate in research activities. The IRB is tasked with upholding the standards for ethical conduct of research and is guided by regulations from OHRP and the FDA. Both agencies focus on the protection of human subjects, but each operates under different CFRs. CFRs are administrative laws published in the *Federal Register* and tasked to agencies for enforcement.

The IRB is authorized to approve, require modification of, or disapprove all research activities that fall within its jurisdiction.

Federal Wide Assurance

Under the DHHS human subjects protection regulations (45 C.F.R. 46.103), every institution engaged in human subjects research that is funded or conducted by DHHS must obtain an Assurance of Compliance approved by OHRP. This Assurance of Compliance, when granted, is called a Federalwide Assurance (FWA) (see www.hhs.gov/ohrp/assurances/assurances/filasurt.html). Both "awardee" institutions and collaborating "performance site" institutions must file Assurances. This document remains on file at OHRP.

Given that PECARN and PECARN-funded studies are supported by HRSA/MCHB within DHHS, each PECARN hospital must have an FWA number or function under a hospital that has a FWA. If a hospital's FWA number in unknown, then locate it by calling the IRB or visiting their website. A copy of the institutional FWA must be stored in the Essential Documents Binder (EDB) at all times (see Section III – The Essential Documents Binder).

Granting Approval

Before granting approval, the IRB must be satisfied that the following criteria are met:

- risks to subjects are minimized by using procedures that are consistent with sound research design and whenever appropriate, using procedures already being performed on the subjects for diagnostic or treatment purposes;
- risks to subjects are reasonable in relation to anticipated benefits to subjects and the importance of the knowledge that may reasonably be expected to result from the research;
- selection of subjects is equitable in terms of the purposes of the research and the setting in which it will be conducted;
- informed consent is sought from each prospective subject and documented to include all appropriate information (see Informed Consent later in this chapter);
- the protocol makes adequate provision for monitoring the data collected to ensure the safety of the subjects;
- adequate provision is made and documented to protect the privacy of subjects and to maintain the confidentiality of the data; and
- where some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as persons with acute or severe physical or mental illness, or persons who are economically or educationally disadvantaged, appropriate safeguards have been included in the study to protect their rights and welfare.

Another criterion all IRBs consider is the Common Rule which includes SAEs. More information on SAEs can be found on the OHRP website (see http://www.hhs.gov/ohrp/policy/advevntguid.html).

Levels of Risk

The answers to the questions in the IRB application will help the IRB determine the risk. Usually, the protocol will clearly address risk to participants. However, if an RC is unsure how to describe risk in an IRB application, consult the PI or the NA or call the DCC.

The levels of risk are defined by HHS Title 45 at www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm (see Table 3).

Table 3: Levels of Risk

Minimal Risk	More than Minimal Risk	
	Direct Benefit	More than Direct Benefit
A situation where the risks, considering probability and magnitude, are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.	Criteria for this level are the same as minimal risk, plus the risk is justified by the anticipated benefit, and the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by other available alternatives. Provisions are also made to protect the privacy of the subjects.	The same as direct but there is no evident direct benefit. One point that is unique to this level is that the research is likely to yield generalized knowledge about the subject's disorder or condition of vital importance for the understanding or amelioration of same.

Subpart D of HHS Title 45 (see www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html#subpartd) details special conditions for research with children. Permissible research includes research that poses:

- not more than minimal risk;
- greater than minimal risk and prospect of direct benefit;
- minor increment over minimal risk and no prospect of direct benefit;
- increase over minimal risk and no prospect of direct benefit – under special circumstances only; and
- significant risk and special opportunity (Secretary of HHS review).

Categories of IRB Review

Three levels of review exist for an IRB: exempt, expedited, and full quorum. The level of risk and type of data collected are used for determining the level of review.

- **Exempt**. This is the minimum for IRB review. According to NIH, exempt studies are conducted in established or commonly-accepted educational settings and involve educational tests that do not identify subjects or put them at risk for any liability.

- **Expedited**. For expedited review, there must be minimal risk to subjects. In this case, the project is reviewed by a designated voting IRB member, as opposed to the entire IRB panel. Expedited review is also used for minor changes to existing protocols.

- **Full Quorum**. Also known as full board review, it is the highest level of review for studies that pose the greatest risk to participants. The IRB board must have at least one nonscientific member present for these reviews. Studies that typically require full quorum include drug interventions, clinical trials, or those that collect information that can be linked back to the participant.

In addition, some institutions require a Prep to Research, which is basically a study to determine the feasibility of a larger study. For this type of approval, the researcher must inform the IRB, either in writing or orally, that the use or disclosure

of the protected health information (PHI) is solely to prepare a research protocol or for similar purposes preparatory to research. The researcher will not remove any PHI from the covered entity, and representation that PHI for which access is sought is necessary for the research purpose. For more information, read 45 CFR 164.512(i)(1)(ii) at www.gpo.gov/fdsys/pkg/CFR-2002-title45-vol1/xml/CFR-2002-title45-vol1-sec164-512.xml.

RCs should review the decision charts provided in Appendix B to help determine the level of review a particular study requires. Although the charts are helpful for determining the level for the IRB, it will be the local IRB that makes the final call. Additional help is available in the OHRP publication Human Subjects Regulations Decision Charts (see http://www.utexas.edu/research/rsc/humansubjects/forms/hhs_decision_charts.pdf).

IRB Forms

Once the level of review is determined for a study, the proper form must be completed. The PI will help the RC complete the IRB form. A few pointers to keep in mind while completing the form:

- Read through the entire form before starting and be sure to follow all instructions.
- Write for the layperson, as the reviewers might not be familiar with a particular field of research.
- Be descriptive regarding the study procedures by:
  - where it will be conducted,
  - study duration,
  - how data will be collected,
  - justification for a procedure if it presents a risk to the subject,
  - how participants will be recruited,
  - confidentiality of information, and
  - risks and benefits of participation.[1]
- Proof-read the entire document for spelling and grammatical errors.
- Be clear; don't be afraid to over-explain a concept.
- Refer to the protocol as much as possible and use language from the protocol.
- Do not change the protocol document and make sure that the correct version of the protocol is submitted.

Feel free to contact the DCC project manager for help in completing the IRB form. If possible, identify a local IRB administrative contact person who can address any questions that arise. Most IRBs are approachable and are open to answering questions, especially when it saves them extra paperwork and correspondence.

IRB Amendments

Once the IRB has approved a project it must be carried out as described in the original IRB submission package. The IRB must approve any additions to or deletions of study procedures or study instruments, regardless of how minor the change(s) may be.

Submitting IRB Documents to the DCC

Once a PECARN study is approved, documentation of the IRB approval must be sent to the DCC. Prior to sending the documentation to the DCC, verify the following:

- Make sure that the letter or web-generated approval states that the study is "approved." Conditional approval, partial approval, an e-mail link to the local IRB system, or a status letter will not suffice as an approval.
- Verify that the letter has an approval date and an expiration date. If it says "one year from now" or the "study may continue," it will be insufficient information to help the DCC determine the expiration of the approval.
- Make sure that the approval includes the study name and version number and version date (if available) and is signed by the IRB chair or designee.
- Ensure that the local hospital name is included in the letter. Letterhead from the "Children's Hospital IRB" creates confusion.

Submit all IRB documentation directly to the study's designated DCC project manager. To identify a site's project manager, access the Data Center Project Assignments database within the DCC public resources eRoom (see www.nedarcssl.org/eRoom/NDDP/DCC). If the study does not have a designated project manager, send all documents to the DCC executive secretary.

Informed Consent Documents

Informed consent is the process by which the participant or the parent learns about a study and makes an informed decision to participate. RCs are often involved in the process of educating patients and parents and in obtaining written consent to participate (see Section III - Patient Recruitment and Retention). A consent document typically consists of the following 18 points (also see OHRP's Informed Consent Checklist-Basic and Additional Elements at www.hhs.gov/ohrp/policy/consentckls.html):

1. A statement that the study involves research.
2. An explanation of the purposes of the research.
3. The expected duration of the subject's participation.
4. A description of the procedures to be followed.
5. Identification of any procedures which are experimental.
6. A description of any reasonably foreseeable risks or discomforts to the subject.
7. A description of any benefits to the subject or to others which may reasonably be expected from the research.
8. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be an advantage to the subject.
9. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
10. For research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained.
11. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.
12. A statement that participation is voluntary. Refusal to participate or subjects request to discontinue participation will involve no penalty or loss of benefits to which the subject is otherwise entitled.
13. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable.
14. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
15. Any additional costs to the subject that may result from participation in the research.
16. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
17. A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject.
18. The approximate number of subjects involved in the study.

Note: When obtaining consent from a child who is old enough to give permission to be included in a study, it is called "assent." While there is no federal mandate dictating the minimum age at which assent is required, many institutions adhere to the "common policy of obtaining assent from children aged 7 and older."[2] The study protocol will define the minimum age at which assent must be obtained from the patient (in addition to consent from the parent/guardian). If an adult gives permission for participation in a study, it is called "consent." Depending on the nature of the study, consent is obtained from both parents.

Waiver of Informed Consent

A waiver of written informed consent can be issued by an IRB if circumstances exist that prevent obtaining consent. In these cases, the RC is permitted to carry out research activities without written documentation of parent/guardian consent. For the IRB to waive the requirement of written informed consent, a study must pose no more than minimal risk to patients.

Documentation of informed consent can also be waived under other circumstances as follows:

- The record for informed consent could be linked to the patient.
- The greatest risk is a breach of confidentiality from identifying subjects from documenting consent.
- Patients will still have the option to have consent documented.
- The study is not subject to FDA regulation.
- Written consent is not typically required for the procedures that will be done for the study.

Exception from Informed Consent

An exception or exemption from informed consent is different from the waiver of consent. As defined above, the waiver allows for written consent to be waived in certain conditions. In contrast, the exception from consent allows for a deviation in the normal informed consent process, meaning consent must be obtained at some point. Be aware that people use the terms "exception" and "waiver" interchangeably but they are very distinct concepts. Conditions for exemption or exception of informed consent according to 21 CFR 50.24 include:

1. When the person is in a life-threatening situation.
2. Attaining informed consent is impossible.
3. Partaking in the research holds out the possibility of direct benefit to the patient.
4. The clinical study could not be conducted without exemption.
5. The proposed study outlines the timeline for treatment based on scientific evidence, and the researcher has guaranteed to contact a legal representative of the patient within the treatment time and ask the representative for consent within the time period instead of continuing the study without consent. The researcher will notify the IRB about efforts made to contact the representative.
6. The IRB has reviewed and approved the informed consent procedures; these informed consent documents are used with patients or their representative in circumstances when possible. The IRB has also reviewed and approved the procedures and information to be given to a family member to disagree with the patient's involvement in the study.
7. The researcher will provide other "protections of the rights"[3] and well-being of the patient.

To see the details of those circumstances where informed consent is not needed, read the FDA's Information Sheet Guidance for Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors (see www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/GuidancesInformationSheetsandNotices/ucm113709.htm).

Submitting a Protocol to IRB

In addition to the federal regulations for research that are outlined in Section II - Research Regulations and Oversight, local IRBs have established policies and procedures for the submission and approval of research studies. This chapter has outlined how to prepare a document for review by the IRB, but the IRB may also have specific questions about how a PECARN study will be conducted, how subjects will be involved, and how data will be analyzed. The RC should always work closely with the PI when completing and submitting an IRB application.

One item that is common to all IRB applications, per the Common Rule, are SAEs. More information on SAEs can be found in OHRP's Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events (see www.hhs.gov/ohrp/policy/advevntguid.html).

IRB Renewals

Regulations require that IRBs review studies annually to assess study progress, enrollment progress, safety issues, study compliance (protocol violations), and any other pertinent issues. This is referred to as an IRB renewal. Usually the IRB will ask for enrollment numbers and any adverse events (AE)/SAE that have occurred. This can be complicated in PECARN as the study is taking place at various sites. The RC should report all AEs to the local IRB as required. Always consult the IRB about how protocol deviations and AEs should be reported.

Remember to submit the renewal with enough lead time to get the IRB approval document to the DCC prior to the expiration of the study. The DCC must have the document in hand prior to expiration (see IRB policy in eRoom).

Study Close Out

A study is considered "closed" by the local IRB when the major study activities are complete. When a study is closed, the IRB will no longer perform an annual review. The term "closed" implies there are no more contacts with patients, access to medical records, nor changes to the data. It is important not to close a study too early. Once a study is closed, the site personnel is no longer permitted to access records, change data, answer queries, or contact subjects. While the DCC and the lead investigator will provide information about closure, the IRB at each site will determine when a study can be closed.

Once a study has completed enrollment and queries and data cleaning activities are complete, the study may be considered for closure. In general, the DCC will email sites when data cleaning activities and study analyses are complete. It may be important to make the distinction that while data analyses at the data center are still underway, the data queries are complete and no more is expected from the site.

Since PECARN data analyses occur at the data center and not at the site, individual site IRBs often choose to close after the site activities related to the study are complete. Other IRBs state that they will remain open until publication of all manuscripts, which could be years for a PECARN study. The local IRB contact will decide whether the study should be renewed or not.

When discussing closure with the local IRB, the RC should be very clear about the specifics of the study. Explain that this is a multi-center study, that the local site has completed enrollment, answered all data queries, and anticipates no more data queries. The RC should also inform the local IRB that the site anticipates no more patient follow up activities or access to medical records. However, the DCC or an investigator may need to inquire or clarify a small piece of data even after a study is closed.

If a study renewal date is approaching at the same time that a study is about to be completed, then consult the DCC or the local IRB for direction on whether to renew or close. Once the IRB has decided to close the study, the RC must forward the closure information to the DCC and, as always, place it in the EDB (see Section III – The Essential Documents Binder).

Things to Remember

The DCC must receive the IRB submission before the stated deadline on all new studies. The DCC must receive the IRB renewal prior to the previous approval's expiration date. A lapsed approval for either could put patients and the study at risk. Send documentation of close-out as soon as received and before the current approval expiration date.

If any of the information is missing from the letter (dates, study name, version date), the PI must issue a letter or e-mail clarifying the information in the approval.

Check with the local IRB or the PI as to when renewals and approvals need to be submitted to make sure ample time is available to get the approvals.

Activity 6: Determining Risk to Human Subjects

Read each case scenario and decide what level of risk (minimal or more than minimal direct benefit/more than direct benefit) it poses to the subjects. RCs should discuss their decisions with other research coordinators.

Case 1. A new educational program for teaching kids and families about asthma was developed and now is being studied for its effectiveness in reducing ED visits. Data collection is done through interviews with parents. Personal data is collected for following up with the participants.

Case 2. PECARN is doing a study that involves asking EMTs and paramedics who come in to the ED how they treat children with sickle cell disease. The study will document what treatment protocols they follow and then call parents within seven days to find out how the parents felt about the care they received in the ambulance.

Case 3. A researcher wants each HEDA site to collect de-identified data (no date of birth, date of visit, etc.) to identify patients that would be eligible for a future PECARN study. This data is sent to the data center and will not be published.

Did the RCs agree on all cases? Most likely they did not. Since PECARN is a network, multiple IRBs must approve each study. It is commonplace for IRBs to disagree on levels of risk or requirement of written informed consent.

Activity 7: Completing the IRB Form

Based on the study description, determine which level of IRB review to expect: exempt, expedited or full quorum.

1. Testing a new medication for seizures: _____
2. Collecting and studying blood samples from healthy volunteers: _____
3. Administration of an anonymous survey: _____
4. Reviewing unidentified digital images: _____

Activity 8: Understanding Informed Consent Waivers and Exceptions

1. Name the PECARN studies that have been granted waivers of informed consent.

_____

_____

_____

_____

_____

_____

2. Name the PECARN study that was granted an exception from consent?

(Hint: A current listing of studies can be found on the PECARN website (www.pecarn.org) under "Current Research".)

_____

References

[1]Tips for filling out your application for nonmedical human subjects research (see http://humansubjects.stanford.edu/research/nonmedical/tips.html), access 8/7/2007

[2]HIC POLICY Regarding: Assent and Parental Permission in Pediatric Research (see www.med.yale.edu/hic/policy/assent.pdf), accessed 9/14/2007

[3]Exception from Informed Consent for Studies Conducted in Emergency Settings: Regulatory Language and Excerpts from Preamble (see www.fda.gov/oc/ohrt/irbs/except.html), accessed 8/6/2007

SECTION III:
SETTING UP AND RUNNING A PECARN STUDY

Chapter 9 RC Professional Responsibilities

The RC is often the first person to speak to a patient and their family about a study. As such, it is important that the RC exhibit professional behavior and respect for individuals at all times.

Addressing ED Staff and Patients

It is recommended that physicians be addressed as "Dr. [Last Name]" in the ED. Nurses should be addressed as "Mr., Ms., or Nurse [Last Name]" unless they prefer otherwise. In front of patients, always use the formal title (Dr., Mr., Ms., etc.) regardless of the level of comfort or personal relationship with that individual. It is best to avoid using nicknames when addressing ED clinical staff in front of patients.

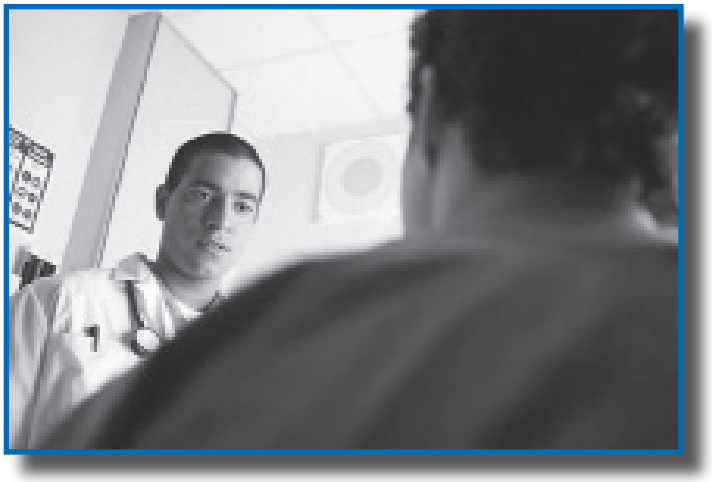
When addressing parents/guardians, ask "Are you John Brown's parent/guardian?" If the parent/guardian responds affirmatively and provides their name, feel free to use it. Otherwise, assume that the patient and their parent share the same last name and address the parent/guardian as Mr. or Mrs. Brown. If a parent/guardian corrects the name, just apologize politely and use the name he/she provides.

Dress Code

In general, PECARN staff members are expected to dress appropriately. Their appearance should not be a distraction or a health/safety concern. A supervisor will let staff members know what attire is appropriate and if dress code requirements exist for a particular site. Frequently, proper footwear that covers the toes is required when working in the hospital environment.

Communication

The RC should be very familiar with the research study and its goals and objectives. Having a solid understanding of a study's objectives and methodology will enhance comfort levels when attempting to describe a study to patients and families. This comfort level will transcend to patients and family members.



If problems related to a study (e.g., protocol violations or unprofessional behavior) are observed, communicate them quickly and professionally to a supervisor, the PI, or the NA.

Professional Development

Many opportunities for professional development are offered to research coordinators. PECARN RCs should be encouraged to take advantage of these opportunities as a means to advance their knowledge of the profession and take advantage of the networking opportunities with other sites.

Professional societies such as the Association for Clinical Research Professionals or ACRP (see www.acrpnet.org) and the Society of Clinical Research Associates or SOCRA (see www.socra.org) offer certification programs for clinical research professionals. Your hospital or institution may offer incentives for obtaining this certification.

PECARN strives to provide opportunities for RC collaboration and professional development. To take advantage of these opportunities, RCs within the network should:

1. attend PECARN Steering Committee Meetings twice annually (see Section 1 – PECARN Steering Committee and Subcommittes). RCs are encouraged to attend the sessions and participate in discussions and provide support for the voting member of their site. Oftentimes it is the RC who is able to provide valuable insight regarding the day-to-day operations of a study and the steering committee looks to RC opinions to answer questions regarding study implementation and maintenance.

2. participate in the RC Advisory Committee. The RC Advisory Committee was organized in 2012 with a mission to provide a forum for RCs to apply their expertise in support of network goals and the efficient management of research studies through collaboration within the sites, investigation of best practices within the network, and providing feedback and recommendations for implementation of research protocols. All RCs within the network are members of the Advisory Committee and are encouraged to attend meetings and phone calls whenever possible. The committee holds meetings in coordination with the PECARN Steering Committee Meetings (in-person or by phone).

3. become an active member of a PECARN subcommittee or study working group. Four subcommittees carrying out specific tasks within the PECARN infrastructure:
   - Protocol Review and Development Subcommittee (PRADS),
   - Grant Writing and Publications Subcommittee (GAPS),
   - Feasibility and Budget Subcommittee (FAB), and
   - Quality, Safety and Regulatory Affairs Subcommittee (QUASI).

   RC members serve on each subcommittee and provide recommendations to the committee. NAs may appoint members to fill open positions in any of the subcommittees

   Study working groups meet in-person and by phone as needed. Generally, a working group is formed to address the issues surrounding a specific study topic and/or study being conducted within the network. During the Steering Committee Meetings, study working group meetings are held during breakout sessions in designated conference rooms. Membership on these committees is usually open to any individuals interested in the topic, and RC involvement is encouraged.

Chapter 10 Research Management

Site Management

An RC's primary responsibility is to track and coordinate all PECARN projects at the site. To ensure ultimate success in facilitating a site's participation in multi-center research, keep the following in mind.

1. **Maintain Regular Communication**. An RC must facilitate communications between the site, the node, the DCC, and PECARN. Quarterly updates, at a minimum, are suggested. The NA and the DCC need to know what's happening at the site so they can: help when problems arise, report progress to the study PI, ensure quality assurance/GCP, and advocate on the RC's behalf when the demands of multi-center research become overwhelming. Additionally, if there are multiple research team members, communications – such as questions or decisions – are best copied to ALL members of the team, including the site study PI, to ensure that everyone stays on the same page.

2. **Attend Meetings**. Meetings and conference calls keep everyone on the same page. They clarify questions, address issues of concern, and keep everyone posted on research progress. If an RC is unable to attend a meeting, he/she should review a copy of the minutes. It is a great idea to follow up any meeting with a confirmation of commitments and action steps identified with emails to participants. Minutes serve this purpose for larger meetings, but for one-on-one meetings, an email summary is very helpful.

3. **Assist the PI**. The RC provides the PI with research and administrative support (i.e., completing relevant research-related paperwork and filing/organizing research documents) as part of the delegated responsibilities of any PECARN study. This support will ensure that the PI's time is focused on clinical/methodological aspects of the study.

4. **Stay on Top of Deadlines**. A major responsibility in site management is tracking research deadlines. Particularly important are deadlines set by the IRB for protocol expiration. Other deadlines may include those set by the DCC for timely data entry and query resolution or deadlines set by a study PI for completion of data collection. The RC should develop a mechanism for tracking important deadlines (a spreadsheet, a system of prioritizing emails, a simple "to-do" list, etc.) and check the system often to ensure deadlines are met.

5. **Prioritize Work**. RCs often find themselves working on multiple projects with competing deadlines. Being able to prioritize workload is key. Deadlines for a manuscript preparation, research presentation, or grant submission should be met first. If an RC is unclear about which project or task should take priority, speak with your HEDA PI, the NA, or the DCC study coordinator for guidance.

6. **Maintain Electronic Files**. The RC's ability to keep track of communications is essential. Having an organized storage system for important emails and keeping a clean email inbox are key elements of tracking communications. An email inbox serves as a tracking system for tasks to be completed and follow-up to be done, as documentation of completed work, and as a source of reference on important study-related decisions that were made. Take the necessary steps now to ensure that all emails are archived and accessible to anyone who will work on the study. Important study tasks or materials should be stored in the EDB (see Section III, Chapter 11 – The Essential Documents Binder).

Keep in mind that storing key communications between the PI, the RC, and PECARN study staff is a regulatory requirement. Key communications should always be stored in hard copy in the study EDB and/or their electronic location, refer-

enced with a memo. With multi-year studies, tracking important communications by paper can be nearly impossible, so archiving emails in an organized, accurately named file structure is an important tool. Email communications should be stored on a secure network drive and should also be backed up to prevent loss of information should the site experience staff turnover.

Study Management

An RC has 10 primary study management responsibilities. For more detailed instruction on each responsibility, refer to the study-specific Manual of Operations (MOO) that is sent to each site prior to study implementation. The MOO includes details regarding: patient eligibility and recruitment; informed consent and regulatory issues; data collection and flow; data entry; recording and encoding; and procedures for reporting adverse medical events (when applicable). The MOO is distinct from the study protocol. It is much more detailed, and attempts to bridge the gap between designing the protocol and actually implementing the study.

1. **Read/interpret Study Protocols**. An RC is responsible for reading and understanding the content of a study protocol so that he/she can convey the necessary information to patients/families and/or train other research support staff.

2. **Complete IRB Paperwork**. An RC is responsible for completing most, if not all, IRB paperwork. The DCC will notify the RC when paperwork is due, such as submitting an amendment because of a protocol change or applying for a continuation if the current IRB approval is about to expire. Protocol changes could also require creating information sheets or the consent form for a study.

3. **Maintain the EDB**. The RC should review the EDB quarterly to look for omissions or expired materials (see Section III, Chapter 11 – The Essential Documents Binder).

4. **Initiate Study Start-up**. Among many other start-up activities, the RC is responsible for helping to train the staff and promote the study (see Section III, Chapter 13 – Research Study Set Up).

5. **Collect Data**. The RC is responsible for the following data collection activities: enrolling patients, reviewing medical records, and administering interviews and/or surveys. Remember the most basic rules of GCP: any time changes are made to a research document, the erroneous information should be struck from the record with one line through the error, and the correct information recorded next to error with the RC's initials and the date of change. Never erase or scribble over information recorded on a research document. If necessary, add a reference such as, "See Note to File or Memo," and add that to the research record as well. The principle of ALCOA (Attributable, Legible, Contemporaneous, Original, and Accurate) is also helpful to realize that what you record and the notes you keep become additional source data for the study. A monitor looking at the notes should be able to understand who wrote the entry and when. Get into the habit of at least adding your initials and the date you recorded this information on the form you are recording it to.

6. **Enter Data**. An RC is responsible for entering data and staying on target with deadlines established for each study.

7. **Comply with Site Monitoring**. Be sure that the site monitor has open access to all necessary source documents in advance of his/her visit (see Section III, Chapter 15 – Site Monitoring).

8. **Attend Study Trainings**. Study trainings may include in-person meetings or conference calls during which important information is conveyed. RCs may also be involved with the study specific training of new study team members (RCs and clinical staff).

9. **Maintain Communications**. The RC must stay in close communication with the DCC study coordinator, the HEDA and site study PIs, and the NA throughout the study. The RC is responsible for reading and understanding the content of relevant email communications and for filing important study communications for future reference. Quite often during a study, clarifications or form updates will be communicated via email and the RC is responsible for staying abreast of these changes/updates. Don't forget to inform all necessary staff of changes to the protocol or consent documents.

10. **Respond to the DCC Queries**. The DCC will send data queries to resolve inconsistencies in data entry. The RC must respond to these queries within the specified timeline or communicate any delays to the DCC study coordinator.

PECARN Performance Measures

In 2011 PECARN developed performance metrics to ensure consistency and uniformity in the quality of its studies throughout the PECARN sites. While the performance metrics change based on the specific or type of PECARN study, they generally address the following areas: patient enrollment process, the IRB process, study data entry, and the ability of a site to meet pre -determined study deadlines. It's important for all members of the site team to be aware of their specific study performance metrics.

To learn more about the study performance metrics and how they should be collected at your site, contact your nodal administrator and/or nodal principal investigator.

Chapter 11 The Essential Document Binder

The EDB, also known as the Investigator Study File, consists of all regulatory records and materials at the participating site pertaining to the study. These documents comprise the site PI's portion of what the FDA and GCP term "essential documents" for the conduct of a clinical study (see table below). These documents permit evaluation of regulatory compliance, conduct of the study, and the quality of the data produced. The table below provides a general guideline for what should be contained in the EDB. The required contents will vary for each study and a study specific guide is usually available in the study eRoom. For questions, please contact the DCC project manager. Although many of these documents are available electronically at the local site, these specific items should be printed out and placed in the binder for easy and quick review during a monitoring visit. It is acceptable to store large or cumbersome items electronically, but a clear link to the location of the item must be noted in the binder.

Table 4: Components of an EDB

Components	What to File Here	Comments/Explanations
Study Protocol	• Record all protocol versions (identify alternate location(s) if not filed in binder)	• Documents that correct protocol versions were submitted
Manual of Operations (MOO)	• MOO (identify alternate electronic location(s) if not filed in binder) • Other supplemental information provided by the DCC or PI • Data collection forms (include sample blank copy)	• Documents any additional information clarifying study conduct • MOO can be electronic
IRB Correspondence	• IRB membership roster • Initial Study IRB application • IRB approval letters (include all approved amendments) • Record of submission and approval dates • Annual progress reports and renewal documentation • Copies of other IRB correspondence • IRB approved Assent/Consent/Parental/Permission forms	• Fulfills regulatory requirements and documents IRB has appropriate certifications • Documents IRB approval and IRB correspondence
Site Correspondence	• Correspondence between the investigator and the DCC • Correspondence between the RC or other study staff and the DCC • DCC correspondence concerning site visits and regulatory and data issues (may refer to eRoom)	• Documents activities and correspondence important to how study is being conducted
Telephone Communications Log	• Telephone log (include alternate location(s) if not in binder) consists of pertinent telephone conversations that a monitor might need to see to understand the study	• Documents any communication regarding an issue you resolved so you will recall later if necessary
Training Documentation	• Documentation of any study training attended by the PI and RC; sometimes this is provided by the DCC	• Documents who was trained and when

Components	What to File Here	Comments/Explanations
Roles and Responsibilities Delegation Log	• A completed Signature and Delegated Responsibilities Form, that describes who is allowed to do what in each study	• Verifies that staff understand duties and what tasks can be delegated
Regulatory Documents	• Federal Wide Assurance for your IRB (FWA) number (available through the IRB Office) • Curriculum vitae (PI and co-investigator, if applicable) and all prior, even if expired or old • Investigator Commitment form • Medical license for PI and all prior, even if expired or old • Confidentiality agreement with the DCC • Current lab certificates • Sign-in log for visitors and representatives	
SAE Documentation/ Safety Reports	• Any Serious Adverse Event reports that were reported and sent to the DCC per MOO directions	
Participant Log	• List of participants, study IDs, MRNs as directed in the MOO	
CAPA, NTF, Protocol Deviation Documentation	• When unusual circumstances or violations from the protocol occur these should be documented in either a Corrective and Preventative Action plan (CAPA), a Note to File (NTF) or a Protocol deviation entry in the database. Notes to file and CAPA documentation should be placed in the EDB	• Documentation of unusual events or communications • GCP irregularities or non-compliance • Explains clearly things that will raise concern if found by a monitor or auditor

Although the EDB may seem tedious, the federal government requires "that the investigator and sponsor of a clinical trial each maintain a complete set of regulatory documents pertaining both to specific patients and to general study records… which was established under the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)."1

The FDA assesses study results through scientific evaluation of data contained in case report forms. While the report forms are a critical part of the investigation records, they usually cannot serve as the complete investigation record.

Activity 9: Discovering the Site's EDB

Find out more about a site's EDB by answering the following questions.

1. Where is the EDB kept at the site?

2. The EDB is for which study?

3. What is the first document in the EDB?

4. Where is the electronic copy of the most recent protocol on eRoom?

5. Who are the clinical staff members on the study?

References

[1]Clinical Trials Management, (http://prevention.cancer.gov/clinicaltrials/management/consortia/step-2/docs), accessed 7/24/2007

Chapter 12 eRoom Monitoring

The DCC is using a commercial software product produced by Documentum, called eRoom, to serve as an electronic, virtual office facility for all individuals involved in PECARN. It can be reached from anywhere in the world via the Internet.

How to Connect

To access eRoom, go to: https://www.nedarcssl.org/eroom/nddp (note the “s” in “https”).

Enter a User Name, which is the user’s first name initial and last name, typed all in lowercase as one word. For example: John Doe would be entered as jdoe. To obtain an eRoom account and password, contact the DCC.

Windows users will be asked to install a plug-in to help run eRoom. This plug-in is not relevant to Macintosh users. The plug-in will allow users to drag and drop files between the Windows desktop and the eRoom pages.

If a user has never logged in previously or if his/her password has been reset, the user will be asked to change their password. Users will have an opportunity to enter a password recovery question, which is a personal question to verify identity.

After typing in the user name and password, press the return or enter key to access the “My eRooms” page. Only the eRooms for which the user is a member will be listed. Click the eRoom name to be taken directly to the main page of that eRoom.

Note: When the user is a member of many eRooms, it is convenient to set up an “Active eRooms” to simplify the process of finding a particular eRoom.

Diagram 3

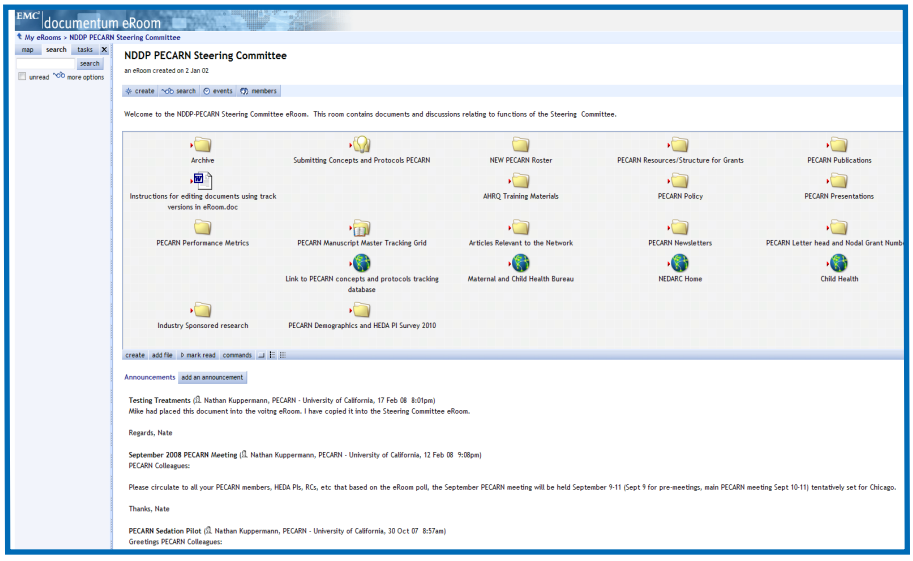
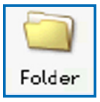


Diagram 4

The PECARN Steering Committee eRoom

The left side is a navigation bar and the rest of the screen is the icon view of the eRoom. The red arrows next to the icons indicate that the user personally has not opened or seen the material. If the red arrow on the top right of the screen is clicked, users will access their first unread item.

Listed below are the icons that can be seen in eRoom along with a brief description of each.



A container in which the user can store, organize, comment, and vote on files, links, and other pages. To add something to a folder, just drag and drop it onto the folder's icon.

A multi-person conversation, where one can read other people's comments and contribute their own. Anyone can create a topic.

A simple text page, with areas for file attachments and comments. Unlike files that have been dragged into an eRoom, notes don't require the reader to have a particular application in order to open them.

A page for taking a vote, where the user poses a question and supplies the possible responses. As people vote, the results are automatically tabulated and displayed.

A team calendar, with month, week, and list views; recurring events; and synchronization to Microsoft Outlook.

A project schedule with a Gantt chart and synchronization to Outlook. The user can group and filter the project tasks, and report actual progress. Each project task can have comments and attachments, like any other eRoom page.

A fully customizable user-defined database for milestones, issues, contacts, or other structured project information. Users can choose fields and data types, and add, sort, group, search, and filter entries. Each entry can have comments and attachments, like any other eRoom page.

A special folder that can receive and store email messages. By cc'ing email messages about a project to an eRoom, the user can create an automatic archive of project correspondence.

A file handled by another application, like a word-processor document or a spreadsheet.

A shortcut to a website, other eRoom, or an individual file or page in an eRoom.

A summary of the information in one or more databases, calendars, or project plans. Dashboards can also appear on the "My eRooms" page.

How to Use Versioning

To upload a new document, drag it directly into an eRoom. Create folders or other items by clicking on the create button inside the eRoom. If a user places a document in the eRoom, he/she is the owner. Once inputted, right-click on the item. This will result in a drop down menu. From here, click on “track versions” to allow eRoom to save all versions of the document. This step is highly recommended.

The “access control” menu item determines who can open, edit, or see the document. To edit a document in eRoom, use this right-click method and select “edit.” The left-click in eRoom, which is the normal mouse click, allows the user to view, but not edit, the document.

Consider the workflow that might ensue with a research manuscript. A draft document would be placed in the eRoom by the original author, who could set it to be visible to everyone in the eRoom, but only editable by one or two people. When an editor wants to work on the paper, he/she selects “edit” in the drop down menu, and the paper will open on their computer automatically. After working on the paper, the editor saves it and it will be placed back in eRoom. The editor will be asked to provide some version information.

While a document is being edited, it is locked and no one else can simultaneously edit it. However, other people can read the version on the eRoom. The real working version should always be stored on eRoom. This eliminates any confusion about who has the most recent version on which computer. By doing this, the user can reach any of their work from any computer in the world. In addition, everyone can take advantage of eRoom’s back up facilities.

eRoom Backup

The eRoom is backed up at the University of Utah every hour during the week, and on a weekly basis a complete backup is stored. For this reason, all network users are urged to store their network-related work on eRoom at all times. There is no reason to keep versions on a private hard drive.

This chapter addresses only a few of the basic features of eRoom. To learn more about the features, functions, and vast possibilities that are available in eRoom, click on the “question mark” located at the top right-hand corner of eRoom.

Chapter 13 Research Study Set Up

Preparing for the start of a new study can be a daunting task, but putting in time up front ensures that the infrastructure and the resources needed to succeed are in place. Some helpful tips for preparing a site for the start of a new study include:

1. **Know the study protocol, the MOO, and the data forms.** After reading the materials thoroughly, it's a good idea to discuss the study design and methodology with the study site PI. The RC must understand why the study is important and what methods will be used to accomplish the study objectives. This is particularly important when beginning a study requiring consent. Knowing the information inside and out will help the RC explain the background, design, and methodology to a patient/parent in language that he/she will understand.

   The RC should ask questions. If something in the protocol or MOO doesn't make sense, it's likely that changes are needed. It's far better to ask a question than to have to correct something later if it is interpreted incorrectly.

2. **Submit the informed consent document to the DCC for review and approval, if applicable.**

3. **Submit an application to the local IRB.** A template IRB application and a protocol will be posted to the study eRoom prior to the start of any new study. On the day that these materials are available in the eRoom, the DCC will send an email alert to all RCs. The email will include a deadline for submission of materials to the local IRB.

   If the local IRB reviews the application and responds with questions or conditions, be sure to alert the PI, the DCC project manager, and the NA as they need to be involved in determining how best to address IRB concerns. Throughout the IRB submission process, the site study PI, NA, and the DCC project manager are key resources.

   One standard study protocol should be used across all PECARN sites. If the research study requires the use of written informed consent, contact the local IRB or look on their website to determine what requirements exist for informed consent documents. The DCC and the PI must review the consent documents before they are submitted to the IRB.

4. **Know the study communications plan.** The study communications plan serves both to introduce an RC to important contact people across the network and to clarify the roles of each study staff person. Following the communications plan will ensure that an RC gets the answers he/she needs with the quickest possible turnaround time (see Section IV: Internal Communications).

5. **Know the study eRoom.** Each new study approved by PECARN will get an eRoom. The RC will receive access to the study eRoom prior to the start of a study and should review all materials posted there regularly to stay abreast of new developments. If eRoom access is not available, notify the DCC project manager or the NA.

6. **Establish a regular meeting time with the study site PI.** The study site PI will be the first and most important point of contact. The RC should establish a regular meeting time up front. The most successful sites are those where the PI and RC meet on a weekly basis.

   Each meeting should include a discussion on enrollment, follow up, and data entry progress; AE/SAE and protocol deviation reporting, if appropriate to the study; and regulatory updates (IRB continuing review, modifications, etc.). The study PI can help explain the medical or clinical aspects of the study and can define important medical terminology.

7. **Schedule training sessions for ED physicians and other relevant staff.** If a study requires the participation or cooperation of ED clinical staff, the RC should schedule training sessions well in advance of the study start date. Train all relevant staff, including the nurses if plans for the study call for them to take vital signs. The RC should also ask to be included on the agenda for department research meetings, hospital grand rounds, or other appropriate training venues. Remember to use the standard training materials provided by the lead study investigator.

   Training should continue throughout the study and can occur in the form of email communications, meetings with research staff to review problems or challenges, or announcements at department meetings. It may be helpful to work with the study PI to develop a communication plan that outlines how frequently the RC will communicate important study information to clinical staff. Be sure to document all of the trainings (including dates, names of patients, and materials used for training) in the training log section of the EDB.

8. **Know the institutional facilities and resources.** The RC should perform an ED walk-round to understand the layout of the department and the flow of operations. Before the study begins, know the following:

   - how to use the ED patient tracking system to screen for eligible patients;
   - how to access the electronic system (for institutions using electronic medical records) and where to look for the ED note, radiology reports, hospital records, and other relevant records;
   - the location of the medical records department (for institutions using paper medical records) and the process for requesting and reviewing records;
   - the roles and training/certification of different ED staff members (especially if relevant to the study); and
   - when and where it is appropriate to approach families and staff for each step of the study enrollment process.

   If the study will require lab work or other diagnostic exams that would not otherwise occur during the course of clinical care, the RC is also responsible for the following:

   - billing any charges related to research procedures (e.g. blood draws) to the research grant. At some institutions this is done by requesting the setup of a research account or bulk account that will then be billed for all research-related procedures. The RC should contact hospital administration or the billing department to clarify the institution's policies.
   - contacting the hospital's Departments of Pathology and/or Radiology. If the research study involves blood draws, the Department of Pathology will likely supply special lab request forms that an RC will either give to the patient, or transport directly to the lab on the day when a patient is enrolled. Likewise, if the study involves obtaining radiology exams, the Department of Radiology will likely establish its own research protocol.
   - working with the Department of Pathology or the hospital lab to ensure that all samples are stored according to established guidelines.
   - asking the PI if it is possible to set up a special order category in the hospital's electronic ordering system. This could be a great short cut for ordering research labs.
   - knowing how to process and ship biohazardous samples properly, if a central lab will analyze the specimens. Some hospitals require special training to learn how to calculate the amount of dry ice necessary for safe transport, etc. Information on the federal regulations related to shipping biohazard materials can be found at: DOHS Biological Materials Shipping (see www.ors.od.nih.gov/sr/dohs/BioSafety/shipbio/Pages/shipping_biological_material.aspx) and UMC Shipment of Biological Materials Manual (see http://ehs.umc.edu/documents/UMMC-Shipment-of-Biological-Materials-Manua_000.pdf).

   If the study involves the administration of an experimental drug, the RC will need to establish a system for appropriate storage and reconciliation of the drug. For example:

   - Consult the MOO or the study protocol to determine any special requirements for drug storage (e.g. sometimes

drugs must be stored at a specific temperature). Taking into account any special requirements, discuss the appropriate storage place in the ED with the PI.

- Notify all persons qualified (according to the study protocol) to handle the study drug where the medication will be located. The drug accountability log should be kept near the medication, and all appropriate staff should be trained on how to complete a log entry for each subject. Establish a schedule to check the log for completeness and accuracy; check for adequate supply of study medications and check medication expiration dates.
- If a study drug must be randomly assigned, understand the randomization process, and explain the process thoroughly to anyone else who is qualified to randomize and administer the study drug.

Note that some hospitals will have an investigational pharmacy on site that will handle most, if not all, of the above mentioned requirements. Be sure to check with the pharmacy to determine what services are available.

9. **Determine how and where to store study data forms.** The RC must determine where to store blank copies of data forms in the ED so that they are accessible to patient enrollers. Determine if electronic copies of the data forms can be stored on the computers in the ED should enrollers run out of printed copies. Consider color-coding the forms to help distinguish between different forms and/or studies at the institution. Always be sure to use the most current version of any data form, as verified by checking the study eRoom. Finally, determine where to place the study lock box so that completed forms can be securely stored until they are collected.

10. **Set up a filing system for the study.** All RCs should design a filing system for patient study files, keeping in mind that any electronic or paper files that include protected health information (PHI) must be stored in a secure manner. For paper files, it is generally required that files be kept in a lock file cabinet behind a locked door. For electronic files, it is generally required that records be kept in a password protected system. Determine if the hospital has any specific requirements for storing electronic data and for the use of portable data storage devices (i.e. laptops and USB storage devices).

    The filing system used should be based on the study methodology. Determine which is best: a chronological system, in numeric order by study ID number, or a customized system based on study activities (e.g. file patients requiring follow-up calls separately from those requiring mail follow-up) or hospital course (e.g. file patients based on their ED disposition).

    Developing a research subject-tracking log can be very helpful in organizing study records. A tracking log, in either paper or electronic format, will provide a centralized place for documenting the progress of each patient through the study protocol. Contact the DCC project manager or the NA for examples of tracking logs.

11. **Determine the most effective and appropriate division of labor.** Review all the research tasks with the PI. Figure out which are appropriate for the RC, for assistant RCs or students, and for the PI. Often times, the responsibilities of each individual involved in the conduct of the research study will be delineated in the protocol or the MOO. Complete the Signature and Delegated Responsibilities Form in the EDB to formally document the roles and responsibilities of each member of the research team.

12. **Prepare the regulatory documents.** Before the beginning of a study, the DCC will provide each RC with an EDB and MOO binder. The RC is responsible for placing all essential regulatory documents in the EDB, and keeping them updated at all times in case of an audit. EDBs come with section dividers, and on each section's cover page is a list of documents belonging to that section. Contact the DCC project manager or the NA for questions about the EDB. Keep in mind, regulatory documents that expire during a study should remain in the EDB and joined by the updated documents. Never discard expired regulatory documents.

The most current version of the MOO can always be found in the eRoom, and should be printed and stored in the MOO binder. All outdated MOO versions should be referenced as an electronic file, and need not be stored in paper copy. Make sure that the MOO is accessible to all individuals working on the study in case the RC is not available to answer questions.

Now that the site is prepared, do a test run. An RC should perform a test run of all procedures (but not with any patients). Carefully review and test out both the data forms and the online data entry system. In the event of a chart review study, order a medical record in advance to ensure the process is understood. Also, the RC should attempt to complete a few study data forms prior to the start of the study to ensure that he/she is able to locate the necessary data points in the medical record, and also to ensure that he/she understands the data forms.

Before beginning an informed consent study, the RC should practice the consent process with the PI to ensure that he/she is able to adequately describe the study purpose, design, and procedures. If other ED staff will be obtaining informed consent, organize a training session where they may all practice describing the study and receive feedback. It is always helpful to review the CFR outlining federal requirements for informed consent prior to beginning a study.

If the study involves the collection of vitals, the administration of a drug, or the use of diagnostic exam, practice the process with all involved hospital staff to ensure everyone understands their role in the research process.

Activity 10: Study Start Up, Don't Reinvent the Wheel

Review the MOO for a PECARN study that was previously conducted at the site and discuss what the RC for that study did to prepare for study start up.

Chapter 14 Patient Recruitment and Retention

How an RC approaches a patient and family can mean the difference between an enrollment and a refusal. Knowing which patients are appropriate to approach for a study is the first step in a successful recruitment process. Although every family presents a unique situation, this chapter provides a few tips that will better prepare the RC for approaching potential patients for a study.

Tip One: Know the study's audience. Knowing the audience will eliminate self-doubt. Knowing the audience means knowing the following:

- Who is eligible for the study? Understand the inclusion/exclusion criteria.
- What is the medical status of the patient? Is the patient medically stable? Should this patient be approached for research? When in doubt, ask the treating or attending physician.
- What is known about the family being approached? Not every patient that meets the study criteria to participate is approachable. Sometimes a patient could look great on paper, but there may be factors, other than those presented in the exclusion criteria, that would eliminate them from the study. For example:
  - an angry or hostile parent,
  - an emotionally distraught parent,
  - an emotionally or mentally limited child, or
  - a child with a concurrent illness that may make the child unfit for the study.
- Does the family speak English? If not, the subject may not be eligible. Check eligibility requirements before enrolling. If allowed, contact translation services to help communicate the study requirements to the family as well as the consent form. To help ensure that true and informed consent is obtained, the RC should use a consent form in the language of the enrollee.
- What is the family's cultural context? It is critical to be aware of and sensitive to a patient's and/or parent's culturally-informed viewpoints, particularly regarding the subject of research and/or medicine. Some people may not believe in research or may be skeptical about medicine in general. Where are patients being approached? Remember, most patients are in an ED setting. By its very nature, this is a highly stressful environment for families. Be sensitive to this fact when approaching patients and their parents.

Tip Two: Focus on relationship-building. One of the most important recruitment tools is being able to build a good rapport with a potential patient and their family. By being knowledgeable about the study and displaying a warm, but professional presence, an RC is more likely to garner the trust of a family. The RC has a very limited time frame to introduce him/herself; provide a brief explanation of the study; and review the consent form, if the parent is agreeable. Positive body language is a must. Maintain eye contact, speak clearly, smile, reach out with a hand during introductions, and retain good posture. These are some of the most effective skills in establishing an immediate relationship with the patient.

Tip Three: Work in collaboration with the providers. Medical care providers (doctors and nurses) are the best link between the RC and the patient. In most cases, the provider has examined the patient and can provide the most accurate information regarding whether a patient meets recruitment criteria, whether he/she is a "do not approach" patient, and/or if there are any other medical issues or circumstances that should concern the RC. In addition, the provider can be a very valuable resource if he/she is able to introduce the study prior to the RC meeting the patient. If the family sees that their physician supports the study, they may be more willing and prepared to listen to an RC, particularly in a stressful situation.

Keep in mind that providers must be informed about the study before patient recruitment begins. Let the provider know exactly what is needed from them regarding the study and why it is needed.

Tip Four: Patient care comes first. Research should never get in the way of patient care. The most important thing to remember is that the reason the patient is in the ED is because he/she is getting treated for an urgent condition. Maybe it's a fever, and although it may not seem emergent, it is to the patient. When the provider comes to treat the patient, the RC should move to the side even if the patient is in the middle of a survey or consenting process.

Enrolling Patients

Follow the 10 steps listed below when enrolling a patient in a PECARN study:

1. Watch the white board or patient tracking system for potential patients. Normally, every study has a screening log to help track the patients that have already been screened/enrolled/permanently excluded.
2. When a patient that meets the criteria is found and the provider has performed an initial evaluation, use the patient's medical record to verify the patient's eligibility. If he/she meets eligibility criteria, go to step 3. If not, add the patient to the screening log as ineligible and state the reason for ineligibility.
3. Find the patient's provider and double-check that the patient does meet eligibility criteria. Again, if the patient meets eligibility criteria, move to step 4. If not, add him/her to the screening log.
4. If the patient meets all eligibility criteria and the provider gives his/her 'OK,' then approach the patient. It is often a good idea to inform the treating team (primarily the physician and nurse) that the patient is being approached about the study. If applicable, it would also be a good time to inform the provider that he/she will need to conduct study procedures if the patient consents.
5. If the patient and/or parent agrees to participate, and has signed the informed consent/parental permission form, then the patient is now a participant in the study. If he/she does not want to participate, add the patient to the screening log as a refusal.
6. When possible, streamline the study process by being prepared. For example, in a study that involves drawing a blood sample and conducting a questionnaire, the RC should ask the provider to draw blood immediately after receiving patient consent. The RC should have everything the provider will need to draw blood: tubes, ice, instructions on how much blood is needed, etc. Then, while the RC is waiting for the blood draw to be completed, he/she can proceed with the survey.
7. Complete all study procedures and study forms as outlined in the protocol and consent.
8. If a follow-up telephone call is required, let the patient know the details of the call: when it will occur, what will be asked, and how long it should take. Obtain the patient's current contact information and the best time to call. Don't rely on medical records for the most up-to-date information.
9. If specified in the protocol and approved by the local IRB, give the patient his/her compensation. Thank him/her for participating in the study.
10. Before leaving the ED, make sure every specimen is labeled as described in the protocol. If there are questions for the provider, ask him/her before leaving.

Obtaining Informed Consent

The RC should go through each section of the consent form with the patient and/or parent. After each section, ask them if they have any questions about what was just described. After reviewing the entire consent document, ask if there is anything else they would like to know. If they have medical questions, direct them to the treating physician. Always offer to give the patient extra time to review the consent document

Practice the Consenting Process

Consider writing a script for the consenting process. It gives the RC the ability to put the consent into his/her own words and helps him/her learn how to consent a patient by conversing and not lecturing. Note that the script is for personal use and should not be used while consenting a patient.

The RC should practice his/her script on someone within the research team. Team members can provide constructive feedback and offer advice on how to better explain items more efficiently. Team members can also play devil's advocate, asking questions a patient may ask, such as who, what, where, when, and why questions.

on their own. Once the patient and/or parent has agreed to participate in the study, an informed consent document must be signed.

Be aware of signs that the patient and/or parent does not understand the consenting process or is only consenting for the compensation. Signs include: a blank stare; saying “yes” to everything, even if it contradicts a previous questions; turning the pages without reading; and having no questions at the end of the consent process. To help increase understanding, consider asking the patient and/or parent questions about study procedures and risks.

The patient and/or parent must complete any information included on the consent form and sign and date the document. Note that the RC must not write in the date or time on the patient’s behalf. Most consent forms also require the parent to initial at the bottom of each page. If a witness to the signature is required, have a nurse, physician, or another RC sign the line as the witness.

The RC should print and sign his/her name as the person giving consent, if required by the IRB or the consent document. Give a copy of the consent form to the family. The original consent form should be placed in the EDB or study files. Make sure that all documents are IRB stamped, if required.

If a separate HIPAA authorization is required, review that document with the patient and/or parent and have them sign and date it.

Make sure that the most current versions of the consent and study documents are being used.

Activity 11: Patient Enrollment

Shadow a current RC while he/she enrolls a patient or create a patient enrollment flow chart for a currently enrolling study.

Activity 12: What Should You Do?

Read the following scenarios and decide how to approach the patient for enrollment.

1. The patient has arrived and appears to meet the study criteria. When the RC enters the patient's room, he/she notices that the family does not speak English.

2. The patient meets eligibility criteria, but the parents are very upset.

3. The patient has a chronic condition, but meets the study criteria.

Chapter 15 Site Monitoring

Site monitoring is an important aspect of a clinical study, whether a double-blind randomized drug trial or an observational investigation. The overall objectives of site monitoring are to:

- verify that the site is correctly following the study protocol;
- verify that all regulatory documents exist and are current;
- document and report on clinical study progress;
- update the site team of any changes in study conduct/documentation;
- ensure that sponsor requirements and investigator obligations are met;
- ensure continued acceptability of the site investigator, team, and facility;
- obtain and review current clinical data, reports, and source documents;
- ensure adequate investigational product inventory and accountability;
- ensure compliance with GCP;
- ensure patient safety; and
- ensure data quality.

Site monitoring generally consists of an on-site meeting involving the monitor, the HEDA investigator, and his/her research staff. Certain aspects of monitoring may also be conducted via telephone, mail, or electronic communication when travel to the site is impractical. Monitoring visits may occur prior to the start of the study (site initiation visit); during the study (monitoring visits); and after study termination (close out visit).

Additionally, sites may get follow up visits as needed based on the study protocol and the site's progress. The regional node center, the DCC, or the PECARN Steering Committee may also request additional visits.

The type of study being conducted will affect the monitoring plan. Retrospective studies and/or chart abstraction studies may require minimal monitoring, but at least one site visit is likely. Observational studies will generally require a higher level of monitoring than retrospective studies, and clinical trials or other interventional studies will require a more rigorous site-monitoring schedule. The size of the study, the number of subjects, study population characteristics, and other aspects of the study protocol should be considered in a monitoring plan.

For more information about site monitoring and why it is an important element to all PECARN studies, view the PowerPoint presentation "DCC Lessons Learned: Site Monitoring in IAI" located at www.emscnrc.org/files/PDF/EMSC_Resources/PECARN_Primer/DCC_Lessons_Learned.pdf.

Site Monitoring Visits

The site will be contacted to ascertain a mutually agreeable visit date. Once the visit date has been decided, an announcement letter is sent to the site (see Sample Site Visit Request Letter). The site letter will outline what will be reviewed at the site. However, the site monitor is not limited to what is outlined. For instance, in addition to the items mentioned in the letter, the site monitor may ask to observe a mock consent process to better understand the consent process at the site (see Sample Site Visit Itinerary).

Along with access to essential documents, the site monitor will expect provision for adequate workspace. The monitor will also expect to have access to key research personnel (e.g. the site coordinator and site PI) during the visit.

Document Review During Site Monitoring Visits

The site monitor will expect access to the following documents:

- **Essential Documents.** The EDB must be complete and well organized. The DCC has provided binders to each participating site to organize and file the regulatory documents, study correspondence, and other essential documents using a format recommended for all DCC trials. Materials can be filed elsewhere with a note of explanation placed in the binder.

  All essential documents must be accessible at the time of the site monitoring visit. For instance, all original IRB correspondence, submissions, and attachments should be provided. Review of these items should provide clear documentation of consent revisions, protocol amendments, and any correspondence with the IRB or any other regulatory body.

- **Source Documents.** Access to the complete, original medical records and other applicable source documents at the site is required. The monitor will review original records pertinent to the time of the patient's enrolment until resolution of any recorded AE or SAE, or to the time of follow up. Source documents will be compared to the data points entered in the study database. It is imperative that sites confirm that there are no institutional restrictions to site monitor documentation access.

- **Trial Database.** Data is usually transcribed from the source document to study database, which contains each protocol specific data point. The site monitor will review data from the source document (medical record or other specified document) and compare each element to what is entered in study database. The site will maintain a patient study file referencing or containing each data point source that is entered in the study database.

  The data point may be taken from protocol specific source documents. For example, blood pressures taken at protocol specified time points, which are not recorded in the medical record. This type of source document must be signed and dated by appropriate personnel.

  When a data point is taken from the medical record, a copy of the pertinent records will be placed in the patient study file. Be sure to copy the full medical record document, including the signature and date of all research and medical personnel. Although copies are not source documents, the copy will help direct the RC to the source data in the medical record for future queries or review.

- **Note to File.** As previously described, the note to file is any written documentation or note that includes information that cannot be recorded elsewhere. It is not a data point per se, and usually requires a narrative.

In summary, the RC should re-examine the EDB prior to the site visit to verify nothing is missing. He/she should also make sure all source documents are signed and dated by appropriate personnel, and all data points entered in study database have a source document (protocol specific source documents, medical record, or note to file). In addition, the RC should re-review data forms and look for identifiable errors. If

Tips for Preparing for A Site Monitoring Visit

- Be up front with the site monitor when asked to provide documents or explain discrepancies.
- Make sure the PI is available to talk with the site monitor.
- Have all documents available or accessible for review. If there is going to be a problem with document access, contact the monitor beforehand.
- Do not be afraid! The monitoring visit is an effort to assure quality of PECARN data.
- Be sure that internet access is available for electronic record access.
- Be organized. Review all documents prior to the monitoring visit.

there are too many data forms to review, pick a sample and look for errors that may have been repeated on other forms. Ask a coworker or the NA to perform a mock site monitoring visit in advance of a formal visit.

Pharmacy Monitoring

For all drug or device trials, the monitor will evaluate records related to the drug or device. The site monitor will, by necessity, be blinded to the study treatment. Therefore, an unblended pharmacy monitor will review drug accountability and pharmacy protocol compliance. In order to maintain the study blind, only appropriate pharmacy personnel will be directly involved in the pharmacy monitoring. Details regarding pharmacy monitoring have been provided in the pharmacy or study specific manual.

Remote Monitoring

In addition to on-site monitoring, the DCC often will request protocol specific quality assurance plans, which include remote monitoring from the DCC. For example, at the start of the study, the site will be asked to fax de-identified source documents associated with the primary data points to the DCC for review. Remote monitoring may also occur annually. For example, the site will be asked to fax de-identified source documents associated with the primary data points for a specified number of patients on an annual basis to the DCC for review. The DCC will provide the site with the patient study database numbers that will be monitored.

The RC should document remote monitoring submissions and correspondence in the EDB. The site monitor will review remote monitoring documentation at the site and perform source document verification for a portion of the primary data points submitted to the DCC.

Site Monitor Visit Report

The site monitor will submit a visit report to the DCC, the protocol PI, the site PI, and the site coordinator. If deficiencies are identified, the site PI is responsible for making corrections. Ultimately, in the unusual occurrence that the site does not respond to the recommendations to improve performance, the network leadership will discuss the appropriateness of the site's continued participation in the study protocol.

The RC should not get upset if his/her site receives a poor monitoring report. A less than perfect monitoring report is always a frustration. However, some of the best sites have been ones that have had the worst reviews. The reason is that a "bad report" sparks change and a better effort at quality assurance at a site.

Sample Site Visit Request Letter

[date]

Site PI [name]
[address]
[city], [state] [zip code]

Regarding: Site monitoring visit for the PECARN protocol [title of protocol]

This letter is to confirm plans for a site visit on [date] from [time] to [time].

The main purpose of this site visit will be to review and verify data and regulatory documents.

I anticipate my visit will take one full day. With this in mind, please reserve a space (e.g. empty office or conference room) for one full day. Also, please arrange a tour of your emergency department.

Please have the following prepared:

1. complete, original emergency department logs and study enrolled/missed eligible/ineligible logs for the following dates in [year]: [dates];
2. access to the medical record system to verify enrolled and missed eligible patients;
3. documentation of PI audit of the emergency department log for eligible patients;
4. CRFs and source document files:
   - All negative CT dictations. Please review, sign, and date these forms and have them available for review at the time of my visit.
   - Completed CRF and source document files for the first five enrolled patients.
5. the Essential Document Binder; and
6. the Manual of Operations.

If you have any questions or concerns, feel free to contact me at [phone and email].

Sincerely,
[site monitor name]
[title]

cc via email: research coordinators
nodal administrator
nodal PI
HEDA PI
study principal investigator

Sample Site Visit Itinerary

Note: This is not an exhaustive list of the items reviewed. This list is meant to give the RC an idea of the level of detail at the monitoring visit.

0900-0930: Arrive at the Site
- inventory the documents provided, ask for documents that are missing
- ask RC "Is there anything you would like me to know before I get started?"
- ask RC to check back with me in a few hours

0930-1100: Review the EDB and MOO
- confirm that approved version numbers are most recent (protocol, CRF, etc)
- confirm Investigator Commitment form is signed, dated, and filed
- review certificates for expiration dates(e.g. medical licenses, human subject protection training)
- review documentation of PI audit of emergency logs

11-1145: Confirm Internal QA Performed by Site (e.g. PI audit of radiology results)

1145-1215: Lunch

1215-1415: Missed Eligible Review
- confirm original emergency department log
- eliminate enrolled patients from review
- record patients from the enrolled, missed eligible and ineligible logs
- review emergency department log, noting any possible eligibles that were not enrolled
- review medical record of possible eligibles
- Does the patient meet Inclusion/Exclusion?
- Was any imaging performed to evaluate for abdominal trauma?
- record missed eligibles not previously reported by site

1415-1515: Meet with RC
- regarding regulatory document review
- regarding unreported missed eligible (ask RC to review the record to confirm that it is an unreported missed eligible)

1515-1545: Meet with PI

1545-1615: Tour ED, Interview RC Regarding Study Processes

1615-1700: Work with RC
- review findings in detail with RC
- make corrections, if possible
- collect missing documents, if available
- teaching points: enrollment criteria, information sheet
- interview RC regarding specific DCC concerns (i.e. time to entry of CRF 6 data)

1700: Depart Site

Chapter 16 Data Management

Collecting study data is one of the most important functions of the RC role. Identifying which data are needed, locating the data in your EHR or medical record, and collecting it on a pre-designed study specific form can be a challenge. Each hospital and ED in the network has different procedures, terminologies, and systems; and all of these affect how data are recorded, saved, and stored. For example, asking for the "first recorded weight" is a loaded question with many possible options: the triage weight, the estimated weight, the medication dosing weight, the ED weight, the admission weight, the parent stated weight, or the historical weight (from when the patient last visited the hospital). This can make a simple instruction like "record the weight here" very confusing.

It is important that you remember that you, the RC, are the main person who will make these decisions when collecting data. If you are unsure, call the DCC or talk to your PI. It can sometimes be very tricky to determine which data element to collect. Second, it can be easy to make a mistake that is perpetuated throughout the entire trial and will later require data re-entry and/or query resolution. The DCC and the study PI work together to develop the data form with RC input. But even so, often RCs identify flaws in the way a question is phrased on a data collection form or database and speaking up about this can be crucial. Do not hesitate to ask questions or clarify directions. An RC's observations from the 'front lines' may be very important in ensuring accurate data collection.

Data Quality

As careful as the RC may be while collecting and entering data, mistakes or misinterpretations are common. The DCC designs and builds quality checks into each study database. The goal is to identify 'dirty' data as soon as possible and feed this information back to the site. There are several ways that this may occur:

- **Site Monitoring Visits.** The site monitor reviews data from the source document (medical record or other specified document) and compares each element to what is entered in the database. If the two do not match, the monitor will ask the site to resolve the problem immediately, if possible.
- **Computer Generated Logic Checks.** Data errors can be found by logic checks to catch data that are out of range, missing, or illogical, such as entering a visit date that is earlier than the date of birth. These checks may send a message directly upon data entry, or the problem may be sent to the site in the form of a data query. Queries fire when data are inconsistent or violate study "rules" that are built in to the data system by the data manager. You will receive queries throughout the study period.
- **Manual Reviews/Remote Monitoring.** The data can also undergo a manual review at the DCC. This method offers a way to monitor the data remotely without the expense of travel.

While there is no magic number to represent an acceptable error rate, researchers want the data to be as clean as possible. An acceptable error rate is considered to be less than 1.0% and sometimes less than 0.5%. Double and triple checking data entry, logic checking, and other methods help minimize error. Data queries help resolve outstanding data errors before the data are analyzed.

Data Queries

A data query is a question directed to the site that identifies any apparent data errors or inconsistencies. If an error is found by a computer generated logic check or by manual review, a data query will be sent to the site from the data center. For ex-

ample, if a four-hour vital sign check was recorded as having been done at 4:00 p.m. instead of 1600 hours, a query would be sent to the site to verify the time. Another example is if a subject had a Glasgow Coma Score recorded as "5" but was reported to be alert. These two variables are inconsistent and would likely result in a query to the site.

The DCC has designed a special system to build and generate queries. The process begins at the start of the study when the DCC or the PI generates logical or clinically-based questions. Each query is written, programmed, and then approved for release by the DCC. Once the query is released, sites receive an email that describes how to correct the errant data and a deadline for completion. Sites either change the variable in the database if it was in error or inform the DCC that the data were, in fact, accurate. If a value is accurate, then the DCC must resolve the query so the automated system will not continue to send a message to the site.

Keep in mind that different issues come up during the course of a study, which may require new queries to be added. In one PECARN study, the DCC determined that sites were possibly interpreting a data variable differently. The DCC and the lead study investigator decided to send out a specific query to evaluate the way this question was being answered. These types of queries can be valuable in assuring that data collection is consistent between sites. Sites will benefit from early queries by catching mistakes in data entry or finding data that are erroneous due to a misinterpretation of the protocol. The DCC welcomes comments from the RCs about queries that do not seem to make sense or are unclear. RC input can help improve a query so that it can be more easily resolved.

The RC is responsible for responding to all data queries. RCs should check the data variable and send a response so the query can be resolved. Once the errant data variable is corrected, the query will automatically resolve and will show up as completed in the query system. In some cases, it is possible that the data are actually correct but just appear to fall outside of an expected set of values. In this case, the RC should inform the DCC that despite appearing erroneous, the value is actually correct. For example, a blood pressure may be outside the range of "normal" but was accurate for a critical patient. This requires requesting a "manual resolve" from the data manager. To do this, you will enter the reason for the discrepant data, for example: "Although the blood pressure was out of normal range, the value is correct. This patient was in cardiac arrest and that is why the value appears out of range." Once a questionable element has been corrected or verified to be accurate, it is considered resolved. Unresolved queries will continue to be sent to the site until they are completed. The network generally expects queries to be resolved in seven days or less. Some queries may be more complicated by nature, and thus take longer to resolve. Sometimes query resolution time is used to measure site performance, so it is a good goal to try to resolve queries as quickly as possible.

Data Collection

Listed below are the top eight mistakes in data collection.

1. **Making Assumptions.** It is easy to fill in gaps in the protocol or the study processes by making assumptions about the way the data "probably" was meant to be collected. It is difficult for a protocol to anticipate site differences; it is also easy to write things that seem clear to the writer, but baffle the person trying to conduct the research. If an RC has any uncertainty about any aspect of the protocol, be sure to ask the PI, the DCC, or the lead investigator. If the RC is unsure if he/she got the right answer from any of those sources, call someone else. Don't give up until the right answer is found.

2. **Rushing the Process.** Often RCs are under pressure to quickly enter data, complete abstractions, enroll patients, or answer queries. Even though PECARN does have to exert pressure at times to meet deadlines, the worst thing an RC can do is rush the process. The research process must be done correctly; otherwise the whole effort is a waste. Leave enough time to complete study activities, especially when entering data. It is easy to spend months collecting data only to enter it wrong when trying to meet a deadline.

3. **Avoiding the PI.** It is tempting for an RC to use his/her best judgment when entering clinical data; it seems rea-

sonable to avoid bugging the PI if possible. But remember, the PI signed an agreement stating he/she would be responsible for all aspects of the clinical study at the site. Clinical data can be very difficult to interpret in a chart; when talking to a parent it can be even more confusing. If an RC has any questions about a data point, it is his/her duty to have the PI verify it. If the data is wrong, the PI will bear the burden. It is the RC's responsibility to make sure the PI knows everything about the study. If the PI says "I trust you," don't give up. Ask the PI to review individual records to ensure things are being done correctly. The RC can also ask the NA for help.

4. **Being a Packrat.** Organization can make or break data collection. Data sheets that have no patient identification, pages that are out of order or missing, folders that are piled up on desks can lead to data errors. In the past, sites have entered results for one patient into another patient's electronic record or lost important data records. Make sure files, papers, and other items are organized, labeled, and stored appropriately to avoid errors and to maintain compliance with regulations.

5. **Ignoring Differences within Study Processes.** Usually study processes are based on how things are done in a single institution (usually the lead investigator's site). If things are done differently in the RC's hospital, then this may contribute to data error. Consider the protocol that says: "after consent, the first set of vital signs should be obtained." Let's say Site A consents the patient in triage and then obtains vital signs before any other routine procedures are done. Site B, however, doesn't have a triage system so vitals are taken when the patient is in the room, which could be several hours after arrival and after medications are dispensed. An obvious difference in the timing of the vital signs could affect study results. Be sure to speak up about study processes that vary at the local institution.

6. **Keeping Quiet about Errors.** The media headlines scream "Scientists Falsify Data," "Researchers Reverse Results," or "Drug Trial's Adverse Effects Emerge After the Trial." So what does an RC do when he/she realizes that data was collected incorrectly or some sort of data error has occurred? Speak up! To err is human, but to keep quiet about an error can threaten the study, the site, and the network. If an RC has lost records, failed to consent someone, or been involved in or witnessed another type of error, he/she must report it.

7. **Averting Internal Communications.** The RC may hear someone say, "Don't contact the DCC, avoid the site monitor, or don't talk to other sites." On the contrary! Having frequent discussions with other sites can help improve processes and reveal ways to improve. Be open about study methods and share great ideas with other sites. Be open and honest with the site monitor. It will only improve data quality.

8. **Drifting Away from the Protocol.** In the beginning of a study, most people follow the protocol exactly, but over time some begin to "drift" away from the rules, making assumptions about what they thought the protocol said instead of re-reading it for clarification. For example, a protocol states that the respiratory rate must be taken within 20 minutes after the administration of medication. Without realizing it, an RC may start collecting respiratory rates within 20 minutes after consent. During data cleaning, the DCC notes that for the last 50 patients, respiratory rate times were taken before the medication was given which is a violation of the protocol.

Another possible protocol violation happens when an RC begins to alter processes based on his/her experience. For example, the RC reads a radiology report and then checks the boxes representing the patient's injuries. In the beginning, boxes are checked only if the injury is listed in the report. Later, as the RC learns more about radiology and injury, he/she learns to look at subsequent radiology reports and read surgical consultation notes. Now when an "equivocal" radiology report is found, the RC looks to the consultant report to see if the specialist noted the injury. If found, he/she checks "yes" for the injury on the data form. The data has now been collected two different ways which may cause differences in data analysis. To avoid this, sites should follow the protocol and develop a written site-specific work flow that clearly states how the protocol will be followed given the specific systems at individual sites. If you have questions, just ask the DCC!

Activity 13: Queries

Ask a current RC to resolve a query.

Chapter 17 Budgeting and Financial Management

Some RCs will have no involvement in financial matters, while others may have significant involvement in grant budgeting and financial management. This chapter is for those who fall into the latter group. It will describe how budgets are set and approved, and how the money is handled once it is awarded.

Setting the Budget

The most common budget process PECARN sites have to work with is through a subcontract or subaward offered to their institution for participation in a study from the lead site that obtained the grant. In the case of the PECARN infrastructure grant, funds are awarded to each RNC, and these sites then have "pass through" subawards with the other two sites of their node.

For every grant submitted for funding, the site seeking funding will contact participating sites to get initial information, documents, and agreement on funding details. Commonly requested information includes: a protocol, the proposed budget, a budget justification, a scope of work, a letter of intent, letters of support, and biosketches from your site's key personnel. If the lead site is applying for a federal grant, they may also ask for a PHS 398 face page and checklist, form 1572, and a Research & Related (R&R) budget spreadsheet. These are NIH forms, and instructions on their usage can be found at Grants.gov. All of this site information is then used to build the grant application for submission. If the grant application scores well and is awarded, the site will receive a Notice of Grant Award and subawards will then be offered to the participating sites.

It is important that someone at each site (the PI or a delegated coordinator) keep track of all correspondences and submitted materials. Each site will have its own internal processes for reviewing these materials and getting them approved by their departments and institution, whether they be paper registration or electronic forms submission to the appropriate personnel for review and approval. Appropriate personnel may include department administrators, section chiefs, grants and contracts, and sponsored programs.

In recent years, two basic budget types are used in grant funding. The fixed cost budget in which funding is specified for salaries, fringes, supplies, shipping, patient care costs, travel, patient stipends, and indirect costs. And the capitated (event based) budget which may include a limited fixed budget and per patient enrolled reimbursement budget parameters. For estimating costs with the grant award, the lead site will project how many patients the site is anticipated to enroll; however, the capitated budget will be a set of terms by which a site earns their additional funding. Many study designs are turning to this kind of budget structure to control costs and incentivize the sites toward enrollment. Each contract is different and should be read carefully by all the appropriate staff at the site to be sure all costs are defined and that the site can afford to participate in the study. Remember, since the institution will ultimately handle and process the funding and billing, the RC must have their official approval of the site's commitment to participate. The resulting project agreement of subcontract is a legally binding agreement between the two collaborating institutions for which the study team will do the work.

Each budget/subaward should be subdivided into periods of 12-month duration (unless partial year funding is anticipated). A period of performance should be specified, since it is essential to ensure accurate budget calculations. A budget summary should be included for proposals with multi-year funding. All budget entries should be rounded to the nearest whole dollar. Once a subaward is signed by both institutions, the site will generate an account number to use for study expenditures and invoicing as appropriate. Someone should be tracking the site's expenditures to ensure that the institution is on budget (not exceeding or missing well-earned reimbursement for the site's study contributions).

Salary and Wages. The salary category in the proposed budget should include the names and/or position titles for all personnel who will be involved in the project, if known. The percent of effort to be applied to the project should also be shown. Total salary costs can be determined by applying the percentage of effort to the current salary rates. An appropriate cost of living increase (e.g., 3% to 5%) should be applied to all salaries for each subsequent year.

Costs incurred for the same purpose in like circumstances must be treated consistently. For example, salaries of technical staff should be treated as direct costs, i.e. can be linked to a specific project. Direct charging of these costs may be accomplished by specifying individual positions within the project budget or through the use of recharge rates or specialized service facilities, as appropriate under the circumstances.

The salaries of administrative and clerical support staff normally should be treated as indirect costs, i.e. not assignable to a specific project. However, it may be appropriate to charge these costs directly to a sponsored project where administrative or clerical services can be explicitly budgeted to a major project and the time and effort of the staff involved can be specifically identified with the sponsored project (see Direct Costs and A-21 for further clarification as to what constitutes a "major project," as defined by OMB Circular A-21). OMB Circular A-21 Principles is included as an Appendix at the end of this document.

Faculty/Staff Benefits (F & B). Staff benefits (health insurance, retirement funds, etc.) are charged to sponsored project accounts either using a rate specified by the institution or based on what it actually cost. This will vary by institution.

Consumable Supplies and Materials. Consumable supplies are items used exclusively in support of project objectives. If it can be demonstrated that such supplies are used only in the conduct of the project and not for other purposes and are consumed completely in the course of the project, such items can be included as direct costs. Items such as laboratory supplies and materials, laboratory notebooks, diskettes, transparencies, printer paper for research data and reports, report binders, and so forth usually can be justified as consumable supplies. However, when supply items are purchases to support the multiple activities of project personnel, they are considered office supplies and cannot be charged directly to federal funds. Such items would include stationary, pens, tablets, file folders, staples, paper clips, etc.

The estimated costs of consumable supplies and materials should be indicated in the proposed budget, including shipping charges where appropriate. It is generally acceptable to sponsors to provide a breakdown of supplies and materials by broad categories as opposed to the detailed listing of individual items. Contracts awarded by industries holding a prime contract with a federal agency, however, may require detailed itemization of supplies.

Equipment. Major items of equipment proposed for acquisition should be itemized by descriptive name and estimated cost, and an adequate justification should be provided in the proposal narrative. Items costing less than $5,000 or with a life expectancy of less than two years normally should be included under “Supplies and Materials.” Shipping and/or installation charges associated with equipment acquisitions should be included in the cost estimates but generally are not itemized.

Other Costs. Funds may be requested from the sponsor to cover travel costs associated with the proposed project. Sponsors often require a breakdown of such travel costs by trip, reflecting the purpose, point of travel, number of persons, number of days, air fare, lodging, meal costs (per diem), and so forth. If foreign travel is contemplated, the proposal should include relevant information (including names of countries to be visited) and justification. Some sponsors have special regulations (e.g., use of domestic air carriers) governing foreign travel.

Costs of preparing and publishing reports of project results should be included in proposed budgets. Since page charges often are billed well after the completion of the research, it may be necessary to secure time extensions to pay these charges prior to the time that the project is closed out.

Other anticipated direct costs should be itemized; for example, equipment rental, maintenance agreements, or off-campus space rental. Telephone services and postage should not be included unless these costs are expected to be major elements

in the project (e.g., telephone surveys). “Miscellaneous” or “contingency” categories should not be included. Items normally considered indirect costs should not be included in the proposed budget unless they are extraordinary (e.g., utility costs required to operate a high-energy particle accelerator). There may be pharmacy setup fees in clinical trials and dispensing fees, as well as lab fees and possibly an IRB processing fee.

Network costs, including the hardware, software, personnel services, public access sites, and other related costs required to enable personnel to share software or data or to communicate electronically with other individuals, are considered to be part of the physical infrastructure and as such are considered indirect costs. However, individual workstations and specialized hard-ware and software attached to the network, which are not available to all users, are not included as part of the network costs and may be treated as direct costs.

Consultants and Subcontracts. Federal agencies frequently establish a maximum daily rate of pay for consultants. The institution must enter into a formal agreement with the consultant prior to the initiation of his or her effort. Consultant agreements are subject to the full recovery of indirect costs at the rate applicable to other direct cost items in the proposed budget.

The entire cost of a subcontract is normally shown as a single line item under “Other Direct Costs.” A formal proposal from the subcontractor – including a statement of work, a detailed budget, period of performance, and key personnel – should be included to support this cost element. The project director should provide an explanation of why and how the proposed sub-contractor was selected, including the number of bids obtained.

Subcontracted effort usually requires a formal agreement between the institution and the subcontractor. Indirect costs are recovered on the first $25,000 as of each subcontract.

Indirect Costs. Indirect costs are the real costs of Institution operations that are not readily assignable to a particular project. Full recovery of these costs is expected on all grants or contracts, up to the level allowed by the sponsor's written policy. Indirect cost rates are determined through negotiations with DHHS and are applicable to all federally-sponsored projects. These rates vary by institution and should be verified during the budgeting process.

The indirect cost rates for federal projects and projects sponsored by industry are applied to a modified total direct cost (MTDC) base. The rates are applicable to all direct costs with the exception of the following items, which are subtracted from the direct cost base:

1. Permanent equipment items with a unit value of $5,000 or more and a life expectancy of two years. Nonexpendable items valued at less than $5,000 or with less than a two-year life expectancy should be budgeted as materials and supplies.
2. Indirect cost rate is applied to only the first $25,000 of each subcontract or subgrant.
3. No indirect cost recovery is allowed on costs for alteration or renovations of facilities included in a proposed budget.
4. Tuition charges are excluded from the base on which indirect costs are calculated. Budget proposals should use the MTDC base that excludes tuition charges.
5. Patient care costs.

Pre-Submission Proposal Approval

In most institutions, every grant or contract application must be submitted for prior approval through the appropriate institutional channels before being sent to the proposed sponsor. The exact procedure for submitting proposals will vary by institution and should be available from the office of research administration. Contact the office of research administration for the policies and procedure at each institution.

In general, the following information will be required:

- **Sponsor Information.** The sponsor is the agency or organization from which funds are being requested. Provide information about sponsor deadline, exact address, and contact information. Pay attention to deadlines to ensure the proposal arrives at the research office before the sponsor deadlines.

- **Direct versus Prime Sponsors.** If an institution is a subcontractor on a proposal being submitted by another organization, the "Direct Sponsor" is the organization from which the institution will receive the funds directly. The "Prime Sponsor" is the original source of funds. For example, if Dr. Smith at Wayne State University is applying for a research grant to NIH and plans to subcontract part of the work to Dr. Doe at the University of Michigan, then the Direct Sponsor is Wayne State University and would be indicated on the "SUBMITTED TO" line as: Wayne State University. NIH should be indicated as the Prime Sponsor. The Principal Investigator should be shown on the subcontract as Dr. Doe.

- **Key Personnel.** Key personnel include the principal investigator and the participating investigators and co-investigators.

- **Principal Investigator.** The principal investigator is the individual responsible for the conduct of the research who also has administrative and financial accountability for the project/grant. The person is usually a faculty member or equivalent; i.e., instructor or higher in the faculty tenure track or a research investigator or higher in the primary research track. It is generally inappropriate for overall project responsibility to be assigned to a postdoctoral fellow, research associate, house officer, or staff member.

- Some grant programs are designed for beginning investigators, such as individual post-doctoral research fellowships. Then the institutional advisor of the fellow ultimately will be responsible for the project and should be named as principal investigator on the documents.

- **Participating Investigators and Co-Investigators.** Projects often involve collaboration of two or more investigators with different expertise. In general, only one individual may be designated principal investigator; however, other faculty members can be listed as participating investigators. Co-investigators can be designated if they will be assigned their own budget (including agreed-upon allocation of indirect cost recoveries).

- **Critical Items.** Certain activities may require further registration/inspection/approvals by appropriate institutional committees for the certification of compliance with federal and state regulations. The establishment of a project/grant may be delayed until approvals are granted for the following activities:

  - Use of human subjects/patients
  - Use of human embryonic stem cells
  - Use of vertebrate animals
  - Use of recombinant DNA
  - Classified research
  - Restrictions on openness of research
  - Use of radioisotopes in or on humans
  - Use of radioactive materials
  - Use of human body substances
  - Use of infectious agents

Subcontracts, Subawards, and Consortium Agreements

When funds awarded to an institution for the conduct of a sponsored project are to be paid to an organization outside of the institution, the arrangement is often treated as a subcontract. The procedures and approvals required to negotiate and establish a subcontract will vary by institution so contact the office of research or contract administration to determine the specific regulations at each institution.

In general, once a subcontract is established, an institution will issue a sub project/grant account for the subcontract. Expenses will be allocated to the grant account in accordance with the approved budget and the subcontractor will submit invoices to the sponsor for payment.

Grant Administration

Post-award grant administration will vary by institution so contact the office of research administration and/or financial operations to determine the specific requirements at the institution. In general, a project/grant account is established after an award is received. The purpose of a project/grant account is to allocate funds, including indirect cost recoveries, to the appropriate department/research unit. Once the grant account is established, the budget should be reviewed and the appropriate salaries and other expenses allocated to that account. The allocation should include only the budgeted items, by category, as approved by the sponsor.

Some sponsors and generally all subcontracts require an invoice from the institution in order for payment to be made. This is a crucial step because if an invoice is not submitted, payment will not be made. Depending on the requirements of the sponsor or subcontract, invoices can be sent monthly, quarterly, or on another interval. Carefully review the subcontract to understand the deadline dates for invoices.

Business Associates Agreements

In general, disclosures from a covered entity to a researcher for research purposes do not require a business associate agreement (BAA), even in those instances where the covered entity has hired the researcher to perform research on the covered entity's own behalf. A BAA is required only where a person or entity is conducting a function or activity regulated by the Administrative Simplification Rules on behalf of a covered entity, such as payment or health care operations, or providing one of the services listed in the definition of "business associate" at 45 CFR 160.103.

However, the HIPAA Privacy Rule does not prohibit a covered entity from entering into a BAA with a researcher if the covered entity wishes to do so. Notwithstanding the above, a covered entity is only permitted to disclose PHI to a researcher as permitted by Rule, that is, with an individual's authorization pursuant to 45 CFR 164.508, without an individual's authorization as permitted by 45 CFR 164.512(i), or as a limited data set provided that a data use agreement is in place as permitted by 45 CFR 164.514(e).

Activity 14: Queries

Answer the following questions in regards to budgets.

1. What do direct costs include?

2. What do indirect costs include?

Chapter 18 OMB Circular A-21 Principles

Office of Management and Budget Circular A-21 sets forth principles for determining costs applicable to Federal grants, contracts, and other agreements with educational institutions. The Circular prescribes which costs are allowable and not allowable for recovery from the Government and of the costs considered allowable, whether the institution most appropriately treats them as direct or indirect. The Circular gives reasonably clear guidance on a subset of these costs.

In summary, A-21 states that the following costs should normally be treated by the institution as indirect costs: the salaries and associated benefits of administrative and clerical staff, office supplies, postage, local telephone costs, memberships, and hosting. Use of the qualifier "normally" gives universities some latitude in interpreting the A-21 guidelines.

In general, the following costs are not allowable as direct charges to federally sponsored projects.

Administrative and Clerical Expenses. Direct charging may be appropriate where a major project or activity explicitly budgets for administrative or clerical services and the individuals involved can be specifically identified with the project or activity. The key is that the project requires support services beyond the normal scope necessary for the typical project. Examples of "major project" where direct charging of administrative or clerical staff salaries may be appropriate:

- Large, complex programs such as General Clinical Research Centers, Primate Centers, Program Projects, environmental research centers, engineering research centers, and other grants and contracts that entail assembling and managing teams of investigators from a number of institutions.
- Projects that involve extensive data accumulation, analysis and entry, surveying, tabulation, cataloging, searching literature, and reporting (such as epidemiological studies, clinical trials, and retrospective clinical records studies).
- Projects that require making travel and meeting arrangements for large numbers of patients, such as conferences and seminars.
- Projects whose principal focus is the preparation and production of manuals and large reports, books and mono\ graphs (excluding routine progress and technical reports).
- Projects that are geographically inaccessible to normal departmental administrative services, such as research vessels, radio astronomy projects, and other research fields sites that are remote from campus.
- Individual projects requiring project-specific database management; individualized graphics or manuscript preparation; human or animal protocols; and multiple project-related investigator coordination and communications.

Office Supplies. This category includes, for example, computers (under $5,000), printers, monitors, fax machines, printer paper, toner cartridges, pens, pencils, legal pads, clips, rubber bands, post-it notes, books, individual subscriptions to journals, notebooks, binders, folders, diskettes, and departmental stationery. The category does not include printing, photocopying and duplication, research publication costs, and page charges, (i.e., these are generally treated as allowable direct charges). The category also does not include laboratory supplies such as lab notebooks, data storage supplies (e.g., CDs, CD jackets and wallets, and zip storage), aluminum foil and plastic wrap for packaging and preserving specimens, and materials required for poster or publication preparation (poster board, photographic supplies, color paper).

The circumstances surrounding the expenses in this category play a major role in determining whether to treat as an exception, i.e., to permit as a direct charge. As an example, computers are necessary to the overall administration of a sponsored project. Purchasing computers for this purpose would generally be considered an indirect cost expense -- part of the normal wherewithal the institution can reasonably be expected to provide for its research staff. Purchasing computers to control and monitor scientific equipment, however, represents a different circumstance or use of that equipment and would typically be allowed as a direct charge.

Postage (stamps). The postage costs associated with the normal administration of the project are generally not allowable as direct charges to the project. Examples include interactions with vendors, routine correspondence with the sponsor, colleagues, and potential publishers, and students. In general however, the costs of overnight shipping and handling (e.g., Federal Express) are allowable assuming they are directly associated with the conduct of the project. The principal reason for this distinction is that the latter can be directly assigned to a particular project relatively easily and with a high degree of accuracy. Stamps are generally purchased in bulk and consumption cannot, in a cost effective manner, be assigned to a specific activity.

Telephones. The costs of local telephone lines used to conduct routine business of the project should not be direct charged to a project. Telephones used for the conduct of surveys are allowable as this would represent an unlike circumstance to routine business purposes. Telephone toll charges are allowable if they are directly related to the project activities.

The University takes the position that cell phones and prepaid long distance calling cards also should not be direct charged to Federal sponsored projects because there is no easy or accurate way to monitor usage to ensure project relatedness.

Memberships. The dues to maintain individual memberships in professional and scientific organizations are not allowable direct costs to federal sponsored projects. They are considered professional development expenses and should be covered with discretionary or personal funds.

Hosting. There are very few cases where hosting is allowable on Federally sponsored projects. These circumstances are stated during the proposal budgeting process and are only allowable when the sponsor gives express consent.

Proposal Budgets

To charge these expenses to a Federally sponsored project, the following two criteria must be met during the proposal process:

1. The costs can be specifically identified with the objectives of the project or activity.
2. The costs are explicitly listed in the University-proposed and sponsor-approved budgets.

The preferred test for permission is explicit approval from the sponsoring agency. For all A-21 sensitive items listed above, the charges should be explicitly justified and explained in the budget and budget narrative section of the proposal. Before any charges will be allowed against sponsored agreements, awards must provide evidence that the budget has sponsor approval. Principal Investigators and their units are responsible for ensuring that costs assigned to the project are appropriate.

To justify A-21 sensitive charges in proposal budgets, the following items should be addressed in the budget or budget narrative:

- Because all projects require a certain level of account reconciliation, correspondence, communications, and office expenses, how does the proposed charge differ from the standard level expected to be provided by the institution for all projects?
- The job title may imply that the effort is dedicated to administrative purposes. Is the nature of the work different from the general administrative work conducted for all sponsored projects? Are the charges necessary to meet the technical needs of the award rather than to support the administrative needs?
- The cost category (e.g., office supplies) may imply that the items are being used for administrative purposes. How will the items be used to meet the technical needs of the project? Explain in detail their relevance to the methods used in conducting the project.
- Can the proposed charges be easily and accurately documented as appropriate to the project? How will this be done?

Post Award Rebudgeting

As an exception, local rebudgeting authority may be exercised by the institution and can substitute for explicit sponsor approval in those instances where 1) the terms of the award allow such post-award rebudgeting flexibility, and 2) the need for the expense was not contemplated at the time the original budget was prepared. It should be noted that in most cases local rebudgeting authority is given only on grants. It is rarely allowed on contracts. On subcontracts, it is advisable to check with the appropriate institutional representative to discuss the local rebudgeting flexibility.

This post-award authority should be used on rare occasions only and should never be used to circumvent the integrity of the proposal budgeting process.

Unacceptable Practices

Unacceptable direct charging practices include:

- Purchasing items simply to exhaust an unobligated balance.
- Rotating charges among projects.
- Assigning charges to a project on the basis of the remaining balance to resolve availability of funding issues or simply to avoid the loss of carry-forward balances.
- Charging the budgeted amount (in contrast to an amount based on actual usage), unless the project allows a fixed price or other type of approved reimbursement method that does not require tracking of actual charges to the project.
- Assigning charges to an award before the cost is incurred.
- Charging an expense exclusively to a single award when the expense clearly has supported other activities.
- Applying a unit "tax" to projects to distribute clerical and administrative expenses.
- Transferring an overdraft from one sponsored project to another, without express sponsor approval.

Audit

All sponsored projects are subject to audit by their respective agencies.

SECTION IV: PECARN'S INTERNAL COMMUNICATIONS STRUCTURE

Chapter 19 General PECARN Communications

Most general PECARN communications are funneled through the NAs whose role is to disseminate and collect information from their nodal members. An investigator, RC, or other individual at a HEDA who wishes to distribute information – whether it be targeted to other HEDAs, RCs, or the entire research network – should contact their NA. The NA will disseminate the information to the hospitals in his/her node and to the other NAs who will do the same in their nodes. The same process will be followed for communication requests that require a response. In these instances, the NA will tally the responses from his/her node and respond back to the requesting NA who then will communicate back to the requesting individual.

Table 5: PI and NA Contact Information

NODE	Principal Investigator	Nodal Administrator
CHaMP	E. Brooke Lerner, PhD (414) 805-0113 eblerner@mcw.edu	Brittany Farrell, MS (414) 805-0110 bfarrell@mcw.edu
DCC	J. Michael Dean, MD, MBA (801) 588-3280 Mike.Dean@hsc.utah.edu	Sally Jo Zuspan, RN, MSN (801) 585-9284, Fax (801) 585-3243 sally.zuspan@hsc.utah.edu
GLEMSCRN	Rachel Stanley, MD, MHSA (734) 936-1724 stanleyr@umich.edu	Sherry Goldfarb, MPH (734) 763-7488, Fax (734) 936-2706 goldfarb@umich.edu
HOMERUN	Richard Ruddy, MD (513) 636-7973 richard.ruddy@cchmc.org	Melanie Hounchell, BA, CCRC (513) 636-0392 Melanie.Hounchell@cchmc.org
PEM-NEWS	Peter Dayan, MD, MSc (212) 342-4176 psd6@columbia.edu	Grant Jones, MSc (212) 305-6728, Fax (212) 342-4180 gj2132@columbia.edu
PRIDENET	Robert Hickey, MD (412) 692-7972 robert.hickey@chp.edu	Karli Wagers, RN, BSN, MSN (412) 692-6739, Fax (412) 692-7464 karli.wagers@chp.edu
PRIME	Nathan Kuppermann, MD, MPH (916) 734-1535 nkuppermann@ucdavis.edu	Emily Kim, MPH (916) 734-0373, Fax (916) 734-5333 emily.kim@ucdmc.ucdavis.edu
WBCARN	James Chamberlain, MD (202) 476-2353 jchamber@cnmc.org	Kate Shreve (202) 476-5303, Fax (202) 476-3573 KShreve@cnmc.org

Chapter 20 Study Communications

PECARN study communications will come from a variety of sources, all of which may include important information. Study communication sources include: the MOO, study training, the DCC project manager, study conference calls, study eRoom, and the site PI.

Manual of Operations. After a PECARN study is approved for implementation by the Steering Committee, and the protocol is fully developed by the study PI and the protocol subcommittee, the DCC will prepare the MOO. The MOO is to be used by the PI, co-investigators, RCs, and data collectors at each participating HEDA to ensure that the study procedures are followed as uniformly as possible.

If the MOO and the study protocol are not in agreement, the study protocol remains the definitive document. If readers of the MOO identify discrepancies between the MOO and the underlying study, they should contact the DCC so that the error may be fixed.

Study Training. Prior to study implementation, a PECARN training session will be held for all investigators and RCs. Study training will provide essential information about the protocol, patient recruitment, data entry and management, and site monitoring. Additional training will be held on an annual or as needed basis.

The DCC also uses Moodle, an online tool, as an additional training resource for PECARN studies. The modules are generally 15 minutes or less followed by a short quiz. Certificates are provided upon completion. To access Moodle, go to https://elearning.utahdcc.org/login/index.php.

In addition to the PECARN-wide training, it is the responsibility of the HEDA PI to ensure that all staff have received adequate training to accomplish the tasks that have been delegated from the investigator to the staff member.

DCC Project Manager. Each PECARN study is assigned a DCC project manager who, along with the study PI, oversees study operations. The project manager will distribute study updates and other study-related communications via email. The project manager also maintains the study eRoom, which includes all information related to the study. The DCC project manager should be the first stop for questions. The DCC has a commitment to respond to site questions as soon as possible, often within 24 hours. If an RC does not receive a response within 48 hours, he/she should contact their NA.

Study Conference Calls. Conference calls will be held on a regular basis for all PECARN studies. It is important for both the site PI and the RC to attend these calls where important information is conveyed. Notification of conference calls will be sent via email.

Study eRoom. An eRoom is maintained for each PECARN study. Upon being assigned to a specific study, the RC will be granted access to the study eRoom. The eRoom will contain important study information including the MOO, study updates, conference call minutes, and frequently asked questions.

Site PI. The site PI is responsible for overseeing all aspects of the study. Previous experience has shown that the most successful sites are those where there is frequent communication between the site PI and the RC. Ideally, the site PI and the RC will meet weekly to address any issues or questions.

Study Communications Flow

When ED staff have a study-related question, they should seek help from the site PI or RC. The site PI or RC should seek the answer by checking the MOO and study eRoom. If the question is not resolved, then confer with the site PI, HEDA PI, or NA. If the question is still unanswered, contact the DCC. For additional help on who to contact with what issue, see below.

Table 6: PECARN Contacts by Issue

Contact	Issue of Concern
Site PI or designated physician	• Patient eligibility decisions • Medical decisions
NA and site PI	• Data collection form clarifications • IRB issues • Unresolved protocol or study procedure questions
DCC project manager	• MOO, essential documents, and eRoom documents • eRoom access • Patient eligibility questions • Data collection form clarifications • Protocol or study procedure questions • Study flow and enrollment questions • Other unresolved issues or questions, particularly concerning reports on missing data, forms, or out-of-bounds values
DCC data manager	• Trial DB access issues • Data entry and transmission problems

The above information is excerpted from the PECARN communication plan that can be found in eRoom.

SECTION V:
RESOURCES FOR THE RESEARCHER

Chapter 21 Researcher Resources

PECARN Bibliography

PECARN produces many publications and abstracts each year. A complete bibliography is available in eRoom.

Program Websites

- Pediatric Emergency Care Applied Research Network - www.pecarn.org
- EMSC National Resource Center - www.emscnrc.org
- National EMSC Data Analysis Resource Center - www.nedarc.org
- eRoom - https://www.nedarcssl.org/eRoom

Federal Websites

- Federal EMSC Program - http://mchb.hrsa.gov/programs/emergencymedical/index.html
- Agency for Healthcare Quality and Research - http://ahrq.gov
- Centers for Disease Control and Prevention - http://cdc.gov
- Department of Health and Human Services - http://dhhs.gov
- Office of Human Research Protections - www.hhs.gov/ohrp/
- Office for Civil Rights - www.hhs.gov/ocr/hipaa/
- Food and Drug Administration - www.fda.gov
- National Institutes of Health - www.nih.gov
- U.S. General Services Administration Per Diem Rates - www.gsa.gov/portal/category/21287

Training

- PECARN Training Module (www.pecarn.org/helpfulResources/pecarnTraining.html) - Learn more about PECARN - its structure and how to submit a study proposal along with testing your knowledge about the network.
- Human Patient Protection Education for Research Teams (http://phrp.nihtraining.com/users/login.php) - This is a free, web-based course for people that are conducting research involving human patients.
- CITI Training (https://www.citiprogram.org/rcrpage.asp) - A training resource that can be subscribed to by an institution and has free access for select trainings.

Research Links

- Study Designs (www.cebm.net/index.aspx?o=1039) - From the Centre for Evidence-Base Medicine, this site reviews different study designs along with the advantages and disadvantages of each.
- The Four Most Common Types of Epidemiological Studies (http://www.facsnet.org/tools/ref_tutor/epidem/four) - A review of the four most common epidemiological studies.
- An Introduction to Clinical Trials (http://clinicaltrials.gov/ct/info/whatis) - Learn about clinical trials, how they are conducted, and the phases each involves.
- Ethical Standards and Procedures for Research with Human Beings (http://www.who.int/ethics/research/en/) - Research ethics from the World Health Organization.

Activity 15: The Bibliography

1. Find the bibliography on eRoom (Hint: Start in the NDDP Steering Committee room).

2. How many papers and abstracts within the PECARN bibliography are authored by someone from the RC's node?

SECTION VI: APPENDICES

A: OHRP Decision Charts
B: Top Ten Things RCs Need to Know to Survive the PECARN Wilderness
C: Acronyms and Definitions

Note

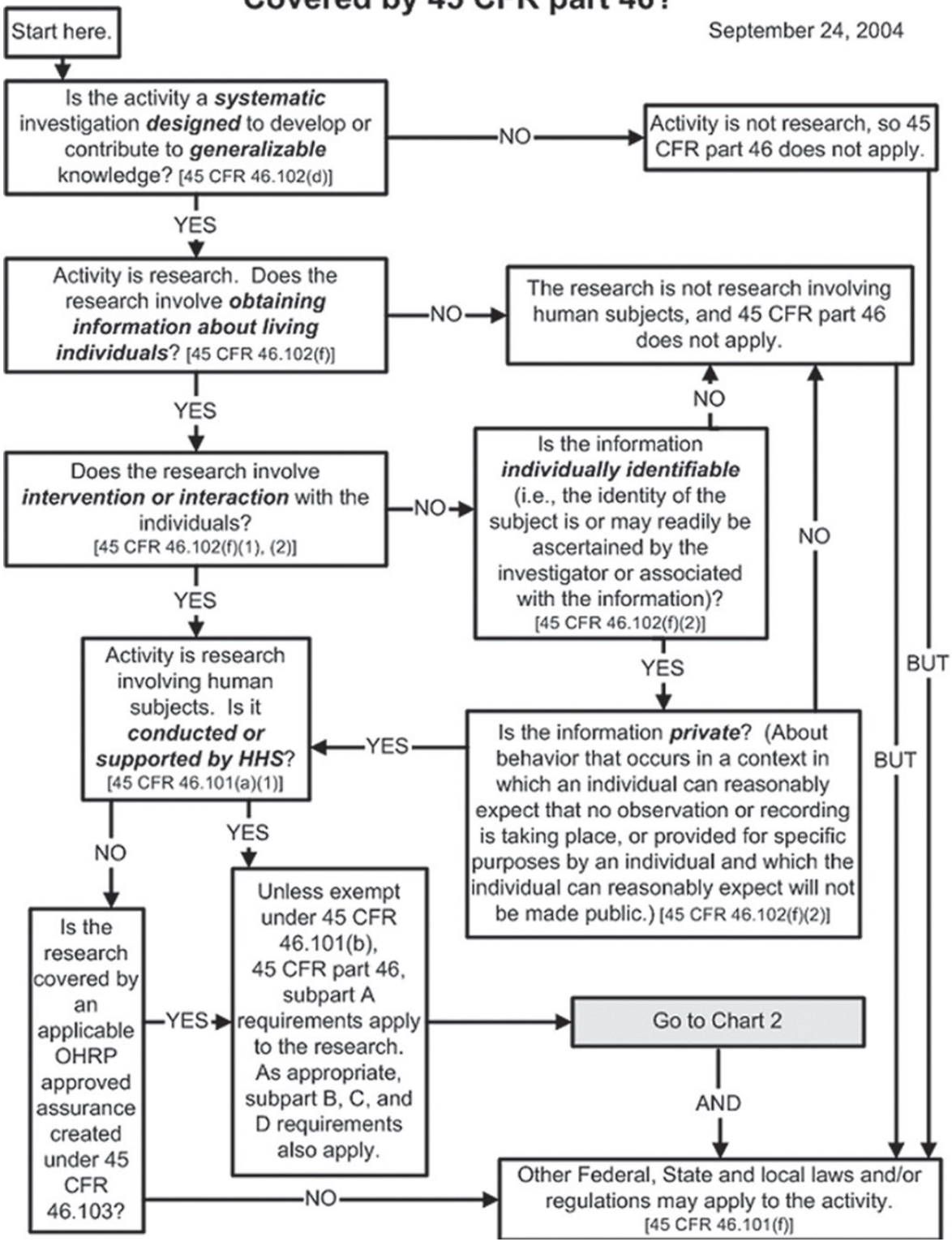
The Office for Human Research Protections (OHRP) within the U.S. Department of Health and Human Services (HHS) provides graphic aids to assist Institutional Review Boards (IRB), research investigators, and others to decide if the research must be reviewed by an IRB based on established HHS regulations. The following decision charts (see Appendix A) address decisions on the following:

- whether an activity is research that must be reviewed by an IRB
- whether the review may be performed by expedited procedures, and
- whether informed consent or its documentation may be waived."

More information about the OHRP Human Subject Regulations Decision Charts can be found at: http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html.

Appendix A OHRP Decision Charts

Chart 1: Is an Activity Research Involving Human Subjects Covered by 45 CFR part 46?



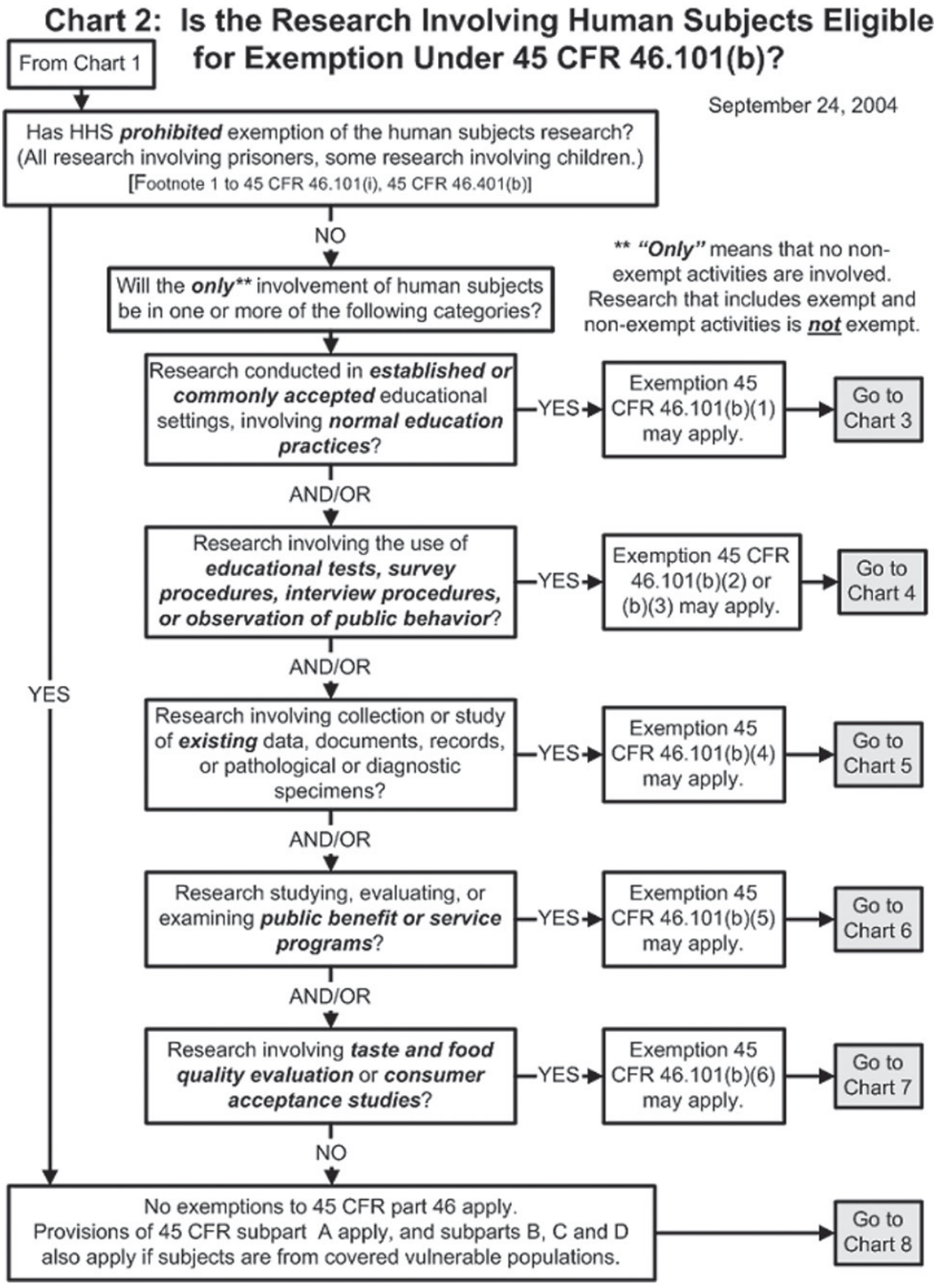
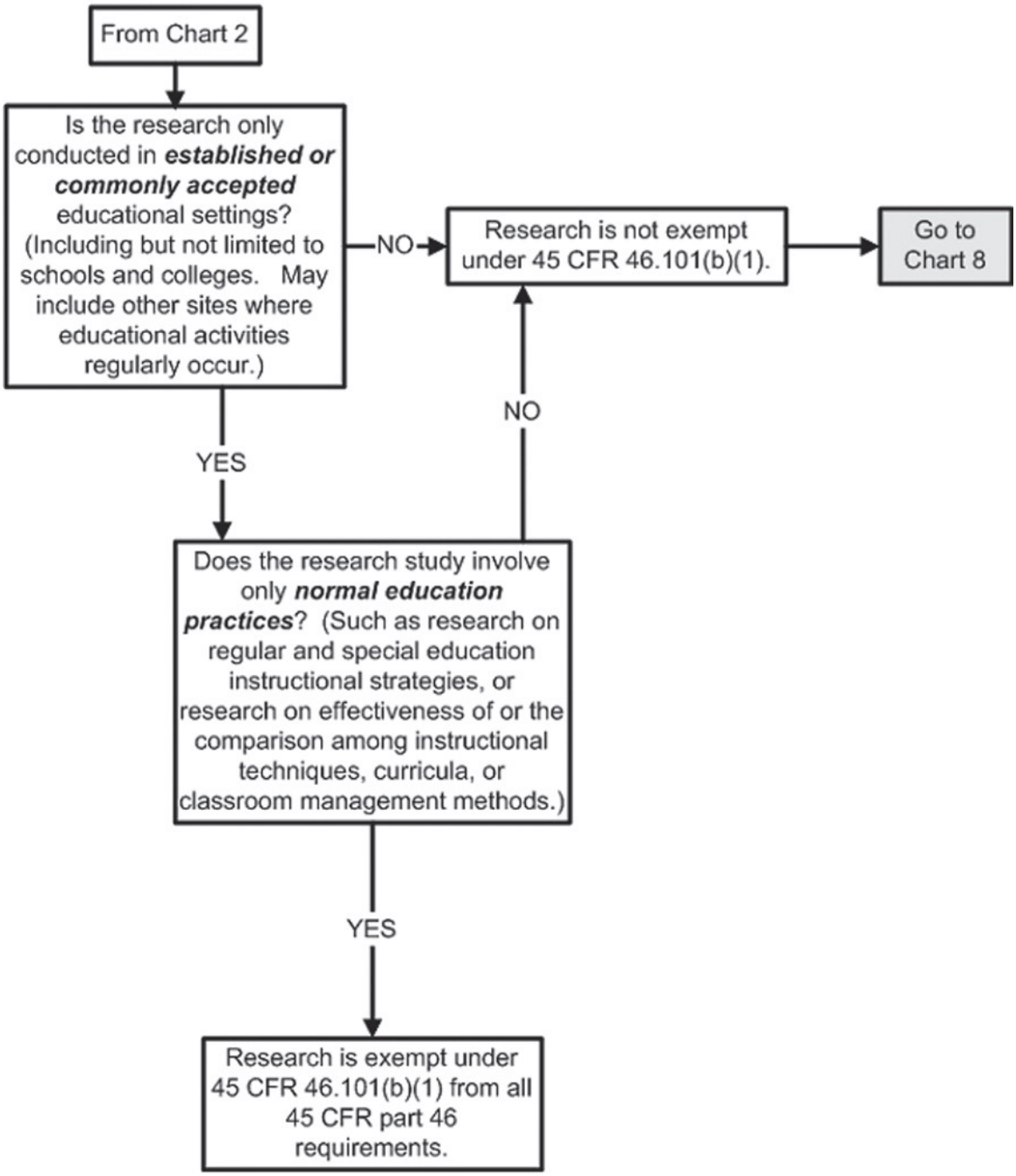


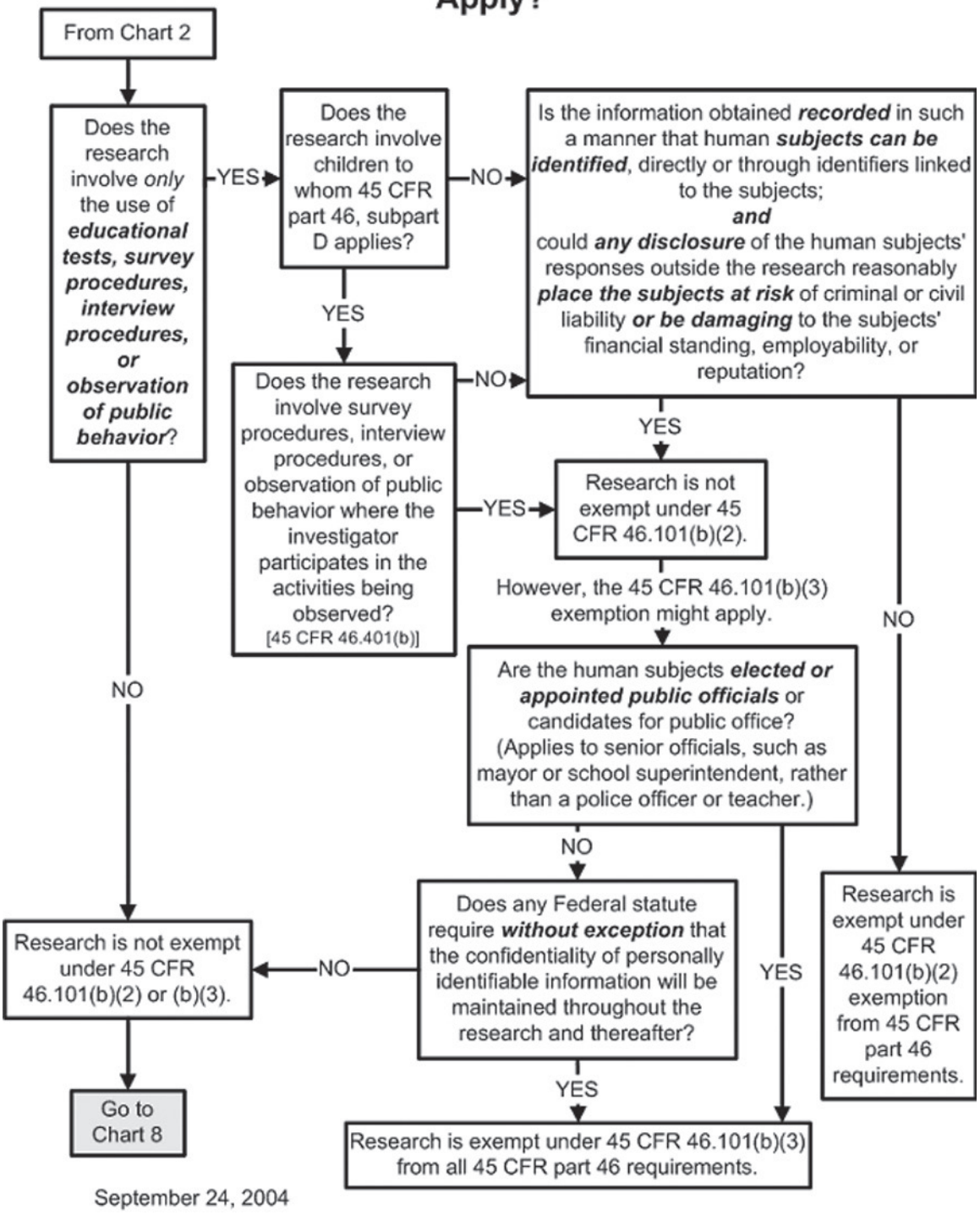
Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?
From Chart 1
September 24, 2004
Has HHS prohibited exemption of the human subjects research? (All research involving prisoners, some research involving children.) [Footnote 1 to 45 CFR 46.101(i), 45 CFR 46.401(b)]
NO
** "Only" means that no non-exempt activities are involved. Research that includes exempt and non-exempt activities is not exempt.
Will the only** involvement of human subjects be in one or more of the following categories?
Research conducted in established or commonly accepted educational settings, involving normal education practices?
YES
Exemption 45 CFR 46.101(b)(1) may apply.
Go to Chart 3
AND/OR
Research involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior?
YES
Exemption 45 CFR 46.101(b)(2) or (b)(3) may apply.
Go to Chart 4
AND/OR
YES
Research involving collection or study of existing data, documents, records, or pathological or diagnostic specimens?
YES
Exemption 45 CFR 46.101(b)(4) may apply.
Go to Chart 5
AND/OR
Research studying, evaluating, or examining public benefit or service programs?
YES
Exemption 45 CFR 46.101(b)(5) may apply.
Go to Chart 6
AND/OR
Research involving taste and food quality evaluation or consumer acceptance studies?
YES
Exemption 45 CFR 46.101(b)(6) may apply.
Go to Chart 7
NO
No exemptions to 45 CFR part 46 apply.
Provisions of 45 CFR subpart A apply, and subparts B, C and D also apply if subjects are from covered vulnerable populations.
Go to Chart 8

Chart 3: Does Exemption 45 CFR 46.101(b)(1) (for Educational Settings) Apply?



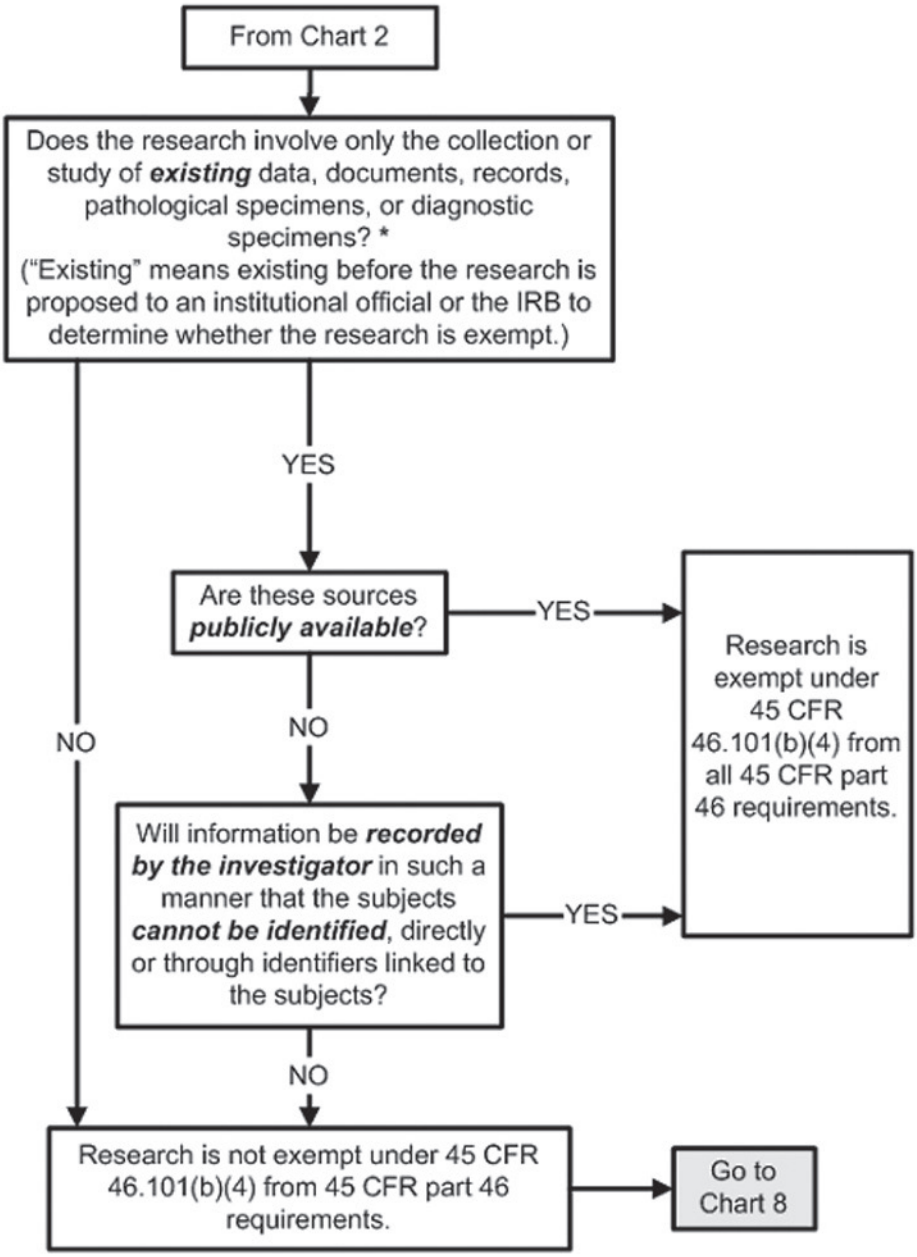
September 24, 2004

Chart 4: Does Exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?



September 24, 2004

Chart 5: Does Exemption 45 CFR 46.101(b)(4) (for Existing Data Documents and Specimens) Apply?



* Note: See **OHRP** guidance on research use of stored data or tissues and on stem cells at http://www.hhs.gov/ohrp/policy/index.html#tissues and #stem, and on coded data or specimens at #coded for further information on those topics.

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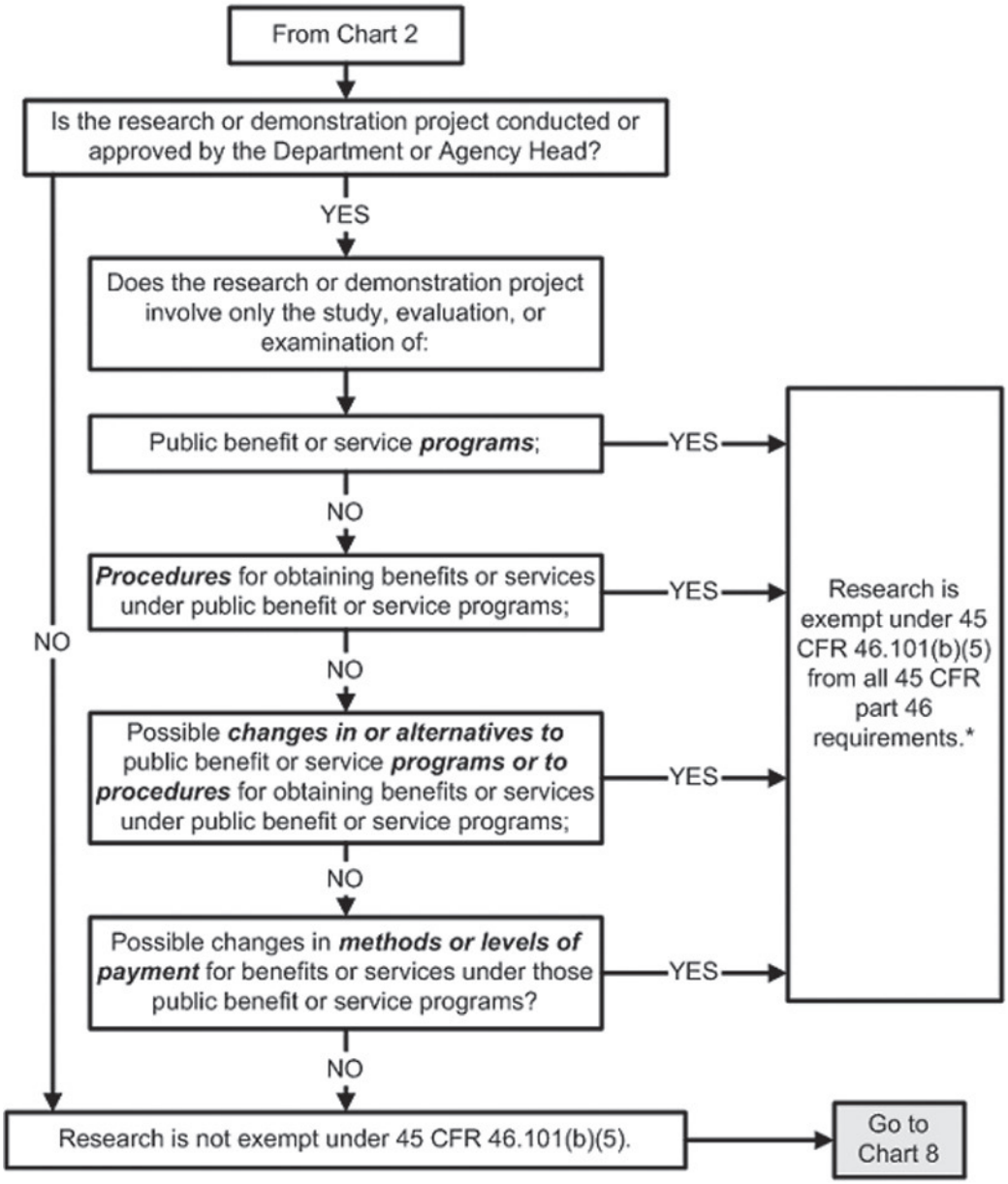
Chart 6: Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) Apply?



* Note: See **OHRP** guidance on exemptions at http://www.hhs.gov/ohrp/policy/index.html#exempt for further description of requirements for this exemption.

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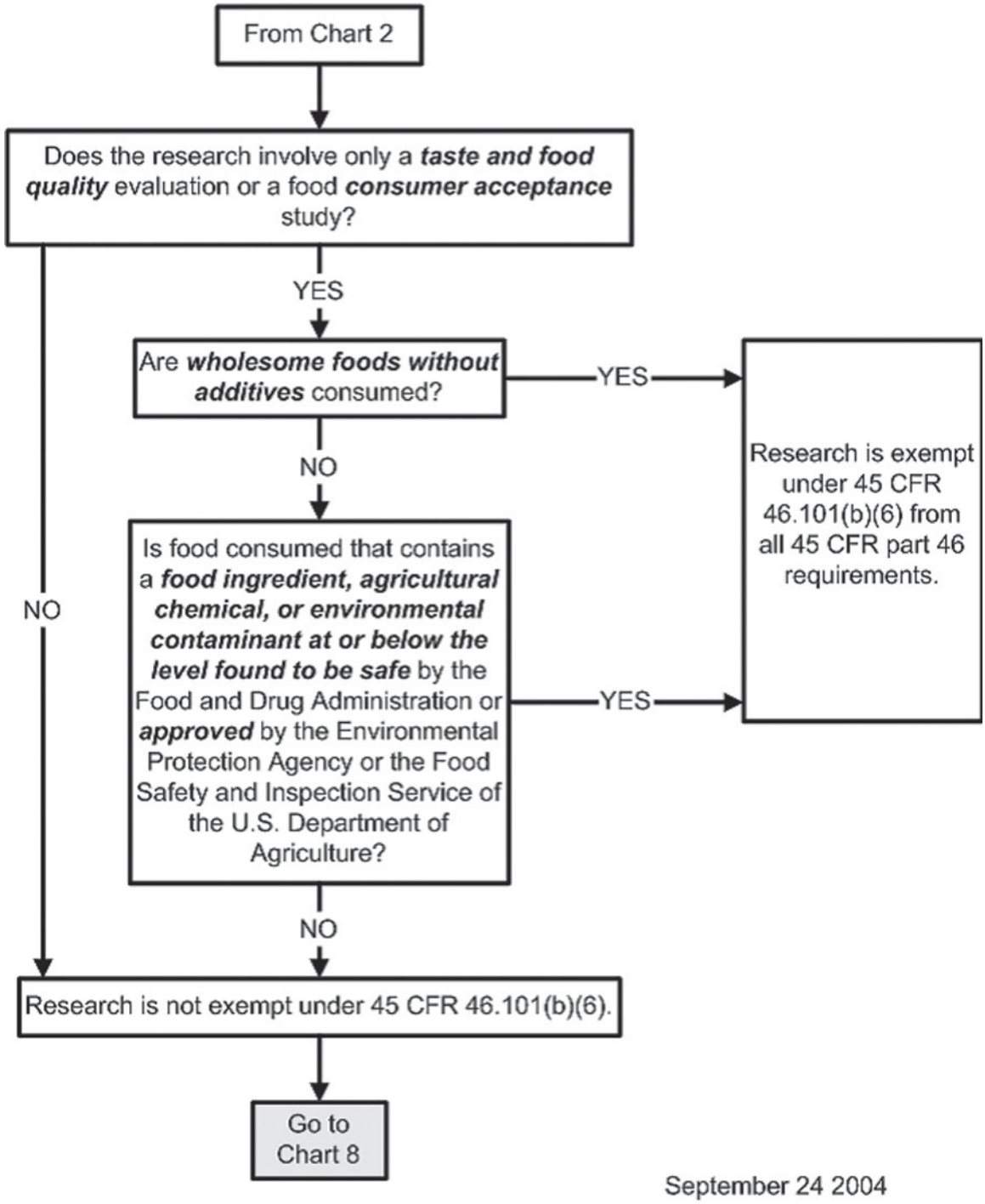
Chart 7: Does Exemption 45 CFR 46.101(b)(6) (for Food Taste and Acceptance Studies) Apply?



September 24 2004

Chart 8: May the IRB Review Be Done by Expedited Procedures Under 45 CFR 46.110?*

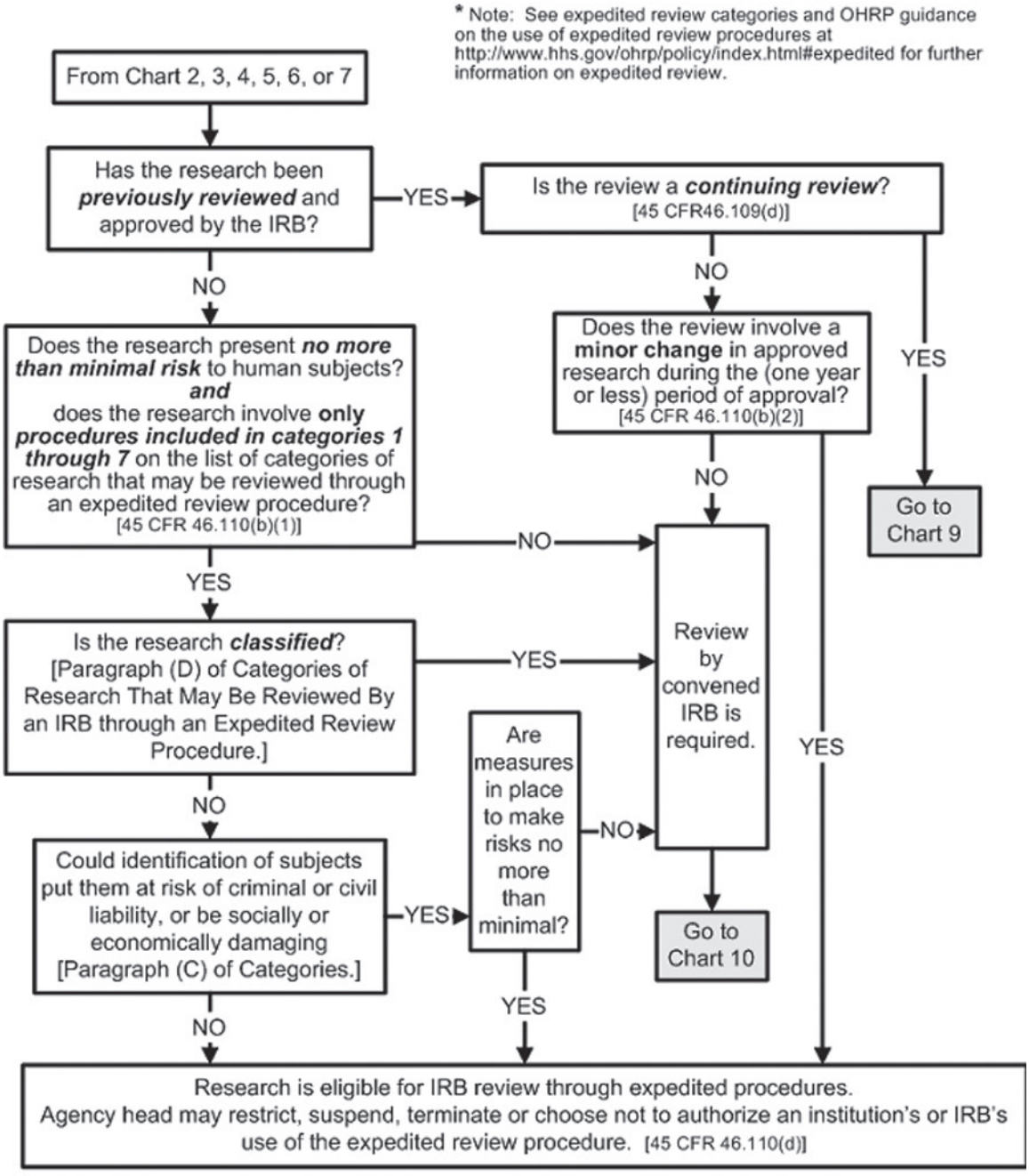


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Chart 9: Can Continuing Review be Done by Expedited Procedures Under 45 CFR 46.110?

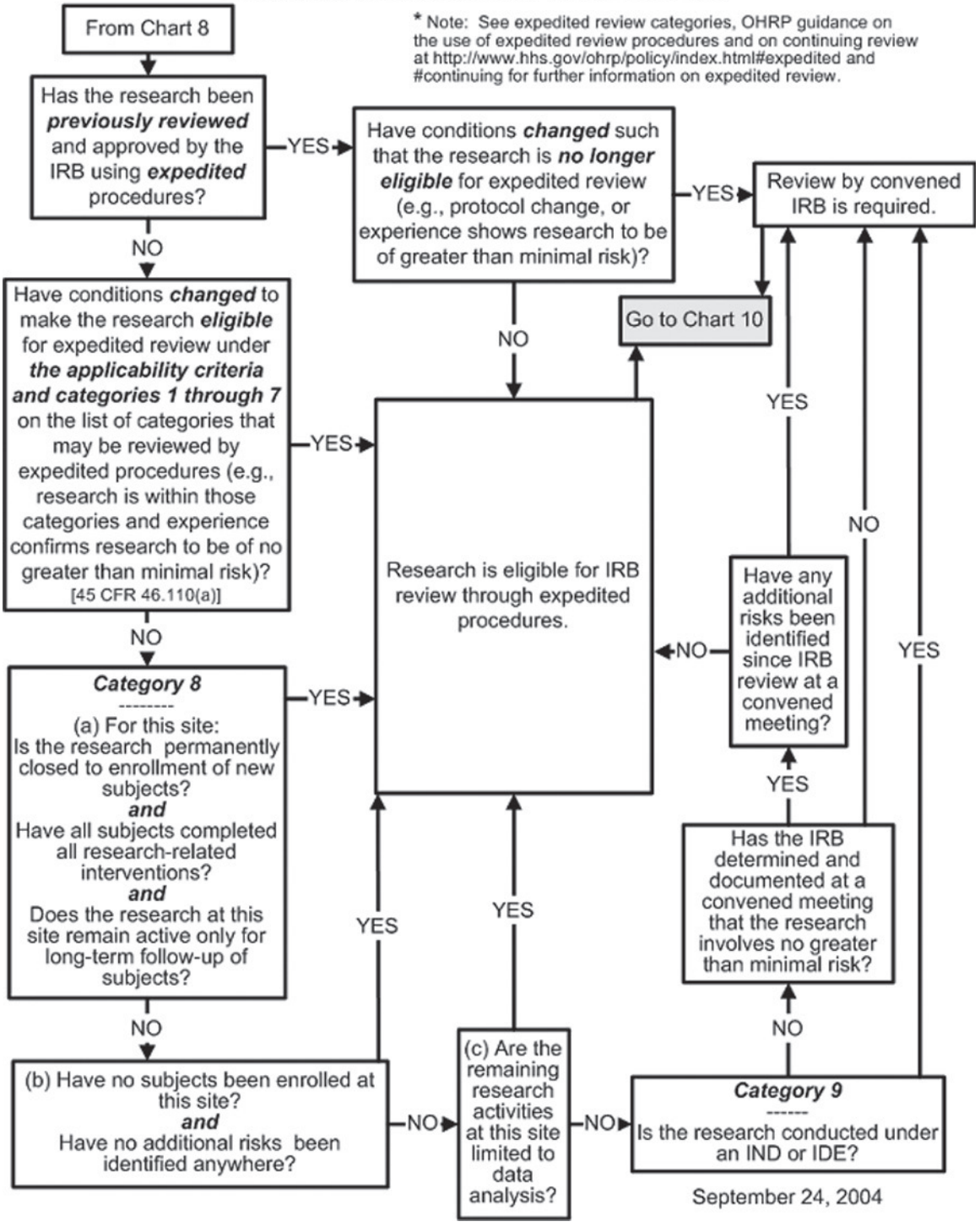
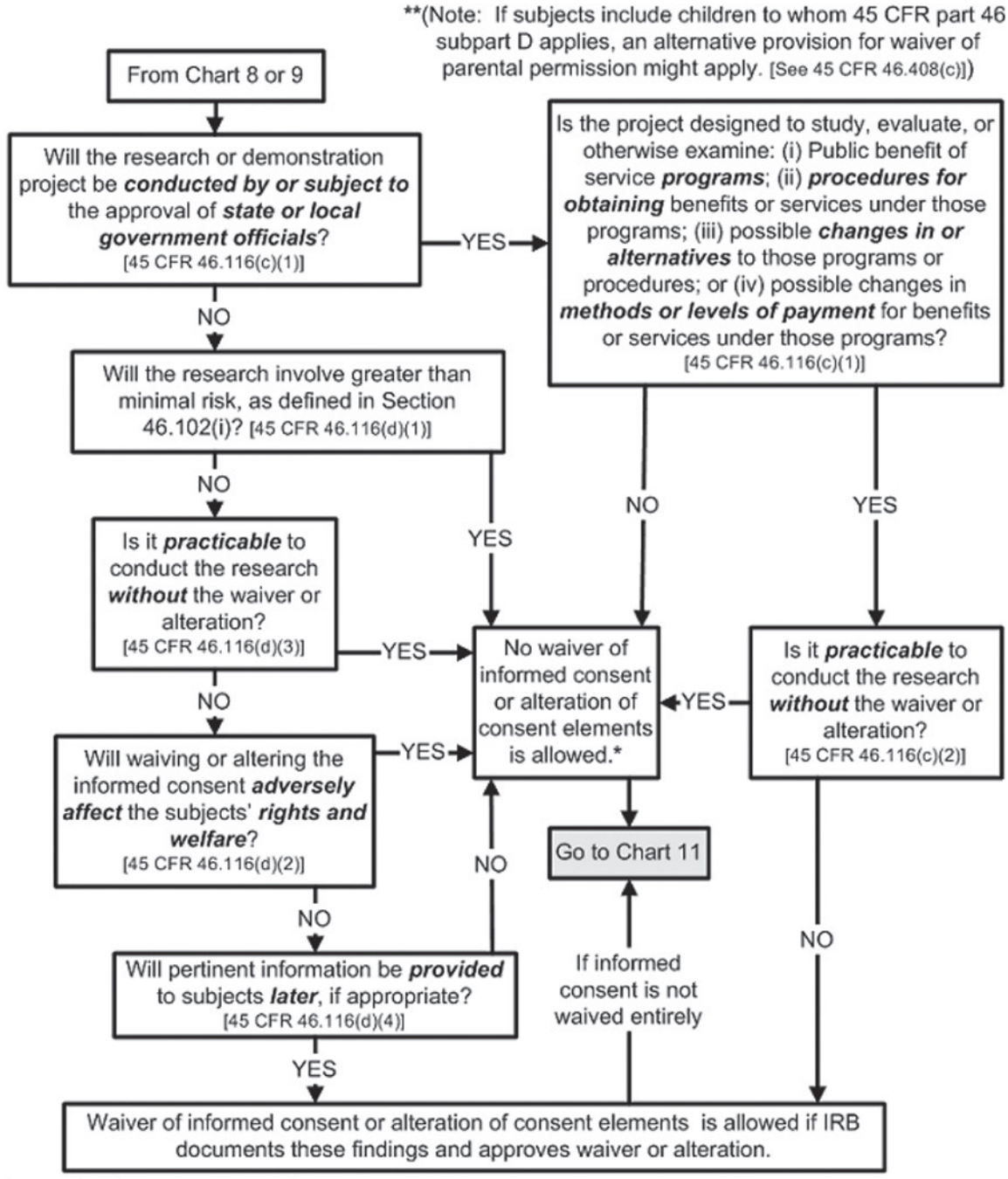


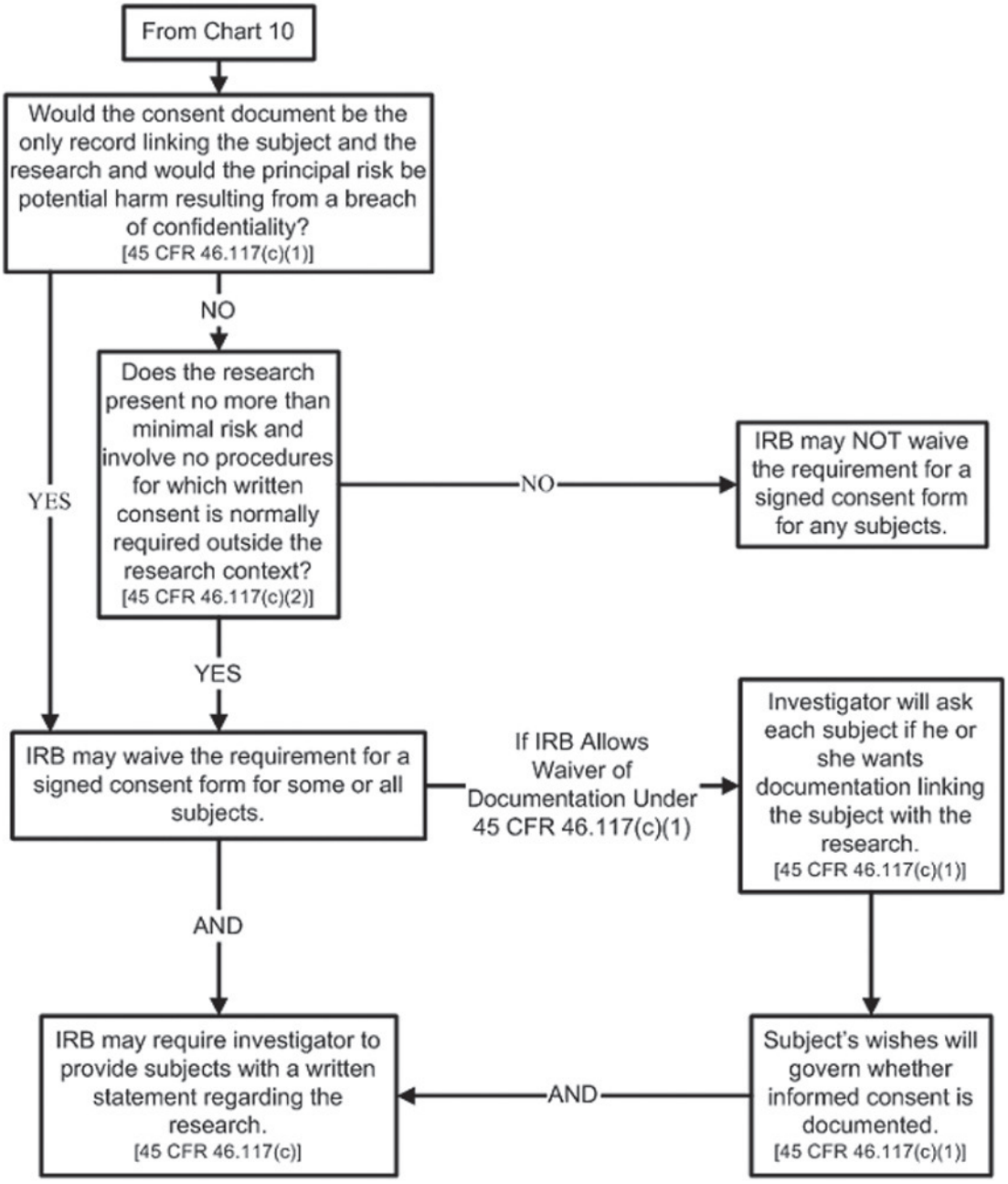
Chart 10: Can Informed Consent Be Waived or Consent Elements Be Altered Under 45 CFR 46.116(c) or (d)?**



* Note: See OHRP guidance on informed consent requirements in emergency research at http://www.hhs.gov/ohrp/policy/index.html#emergency for further information on emergency research informed consent waiver.

September 24, 2004

Chart 11: Can Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?



September 24, 2004

Appendix B

Top 10 Things RCs Need to Know to Survive the PECARN Wilderness

#10 No, this is not ESL this is a PECARN meeting!

- ACORN, GLEMSCRN
- PECARN
- TBI
- IAI, IAF

#9 You're not a Super Hero . . . Get over it!

- Researcher Coordinators tend to be over-achievers and sometimes we just need to step back, breath, and take a break – the work will be there when you get back
- If you do make a mistake
  - Fessing up is not always so bad- you should do it frequently.
  - Chances are, if it happened to you, it has happened somewhere else (and the DCC is gonna find out)

#8 Know when to "drop names"

- Some things are best done by the PI, when appropriate, allow investigators to make contacts and build bridges.
- Sometimes people don't want to help you at all. That is when you cite your PI's name. Hint: It is helpful when your PI is the medical director or division chief (Mike Dean's name also comes in handy at PCMC)

#7 If a tree falls in the forest and you didn't document it

- Documentation is key to everything you do.
- At first, it seems logical that you will just remember things, but when you enroll your 1000th patient, things kinda blur together.

#6 7am comes upon you fast, even on the west coast.

- Remember this when Rachel Stanley wants you to go dancing
- Taking "one more stroll down bourbon street" with your PI does not get you more sleep.

#5 Everything you need to know you learned in Kindergarten!

- Your name and date are sometimes the most important things to remember
- Initial and date all changes, even if seemingly insignificant
- This is the hardest thing to teach to student Research Assistants (even though they presumably have passed kindergarten)

#4 The Voice of Reason is YOU!

- Clinicians do not always see Research in the same light as you do (clinical perspective and workload are factors)
- Clinicians are very busy and need to be reminded frequently about things that are not part of their usual job description
- Don't be afraid to point out things that you think may be obvious (ie: no we can't collect that sample without consent!)

#3 Pack Rats have got it right

- Do not throw away ANY piece of correspondence even if it seems insignificant!
- This will NEVER fail to come back to haunt you

#2 Queries are like bunnies, they multiply when you are not looking (and even when you are)!

- Keep in mind that having a lot of queries means you have entered a lot of data. This correlates to success, not defeat!
- Don't take it personally. It may seem like everyone thinks you are lying, but they just want clean data and they are really on your side!

#1 OCD is your best friend

- No longer a disability, OCD impulses should be yielded to frequently! Embrace your inner OCD!
- Check, double check, and don't be afraid to recheck your facts

Appendix C Acronyms and Definitions

Frequently Used Terms and Acronyms in EMSC

A

Abstract	A summary of a journal article, presentation submission, or grant application.
ACLS	Advanced Cardiac Life Support, includes electricity (defibrillator) and drugs for life threatening conditions.
ACEP Guidelines	American College of Emergency Physicians Guidelines.
Acute care	Providing or concerned with short-term medical care especially for serious acute disease or trauma (e.g., ED, trauma center) Part of the Continuum of Care.
ADA	Americans with Disabilities Act of 1990
AE	Adverse event
AED	Automated external defibrillators deliver an electrical shock to the heart to restore its normal rhythm, enabling oxygenated blood to circulate to vital organs. Once only used by medical personnel, the public now has access to them.
Ambulatory care	Medical care (including diagnosis, observation, treatment and rehabilitation) provided on an outpatient basis.
AHRQ	Agency for Healthcare Research and Quality
ALS	Advance Life Support providers administer certain life-saving medications, perform advanced monitoring of heart rhythms, and are trained to perform advanced procedures to open and manage a patient's airway. They include EMT-Paramedics and EMT-Intermediate (EMT-I) and Cardiac Rescue.
APLS	Advanced Pediatric Life Support, an educational program for physicians.
Appropriations act	Act of a legislative body that makes funds available for expenditure with specific limitations as to amount, purpose, and duration.
Authorization act	Legislation that empowers an agency to implement a particular program and also establishes an upper limit on the amount of funds that can be appropriated for that program.

B

BAA	Business associate agreement
Block grant	A consolidated grant of funds, formerly allocated for specific programs, that a state or local government may use at its discretion for such programs as education or urban development.
BLS	Basic Life Support; includes CPR and removal of foreign body airway obstruction

Broselow tapes	Short for Broselow-Luten emergency tape, a color-coded system used to simplify the use of medications and equipment in pediatric emergency settings
C	
Call for Abstracts	An announcement for potential presenters to submit summary statements of their presentation to a review panel for consideration.
Categorization	An effort to identify the readiness and capability of a health care facility and its staff to provide optimal emergency care.
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation Research
CFR	Code of Federal Regulations
CITI	Collaborative Institutional Training Initiative
Color-Coding	A strategy designed to eliminate errors in the treatment of children related to wrong dosages of medicines, incorrect amounts of fluids, and wrong sizes of equipment.
Continuum of Care	A "seamless" system of care that includes prevention, prehospital care, ED care, inpatient and critical care, and follow-up care including rehabilitation.
Contract Officer	A person with the authority to enter into, administer, and/or terminate contracts and make related determinations and findings.
Cooperative Agreement	A financial assistance mechanism to be used in lieu of a grant when the awarding office anticipates substantial Federal programmatic involvement with the recipient during performance.
CODES	Crash Outcome Data Evaluation System
CPR	Cardiopulmonary resuscitation, which involves breathing for the victim and applying external chest compression to make the heart pump.
Critical Paths	Documentation of essential steps in the diagnosis and treatment of a condition or the performance of a condition, and development of a standard pattern of care to be followed for each patient.
CSHCN	Children with Special Health Care Needs
Cultural Competence	Integration of culturally-sensitive approaches to products and services. Sensitivity addresses language barriers, geographic differences, and other culturally-based distinctions.
D	
DCC	Data Coordinating Center
Demonstration Projects	A federal term for grant-funded projects designed to demonstrate on a particular issue, for a stated period of grant funding.
DHHS	Department of Health and Human Services
Discretionary Funds	Any funds whose distribution is not automatic. Decisions on the distribution of discretionary funds are usually made by an agency on the basis of that agency's choice or judgment and in accordance with criteria set out in law or regulations.

DNR	Do Not Resuscitate, which is requested or ordered for terminally ill patients.
E	
ED	Emergency Department
EDAP	Emergency Departments Approved for Pediatrics
EDB	Essential Documents Binder
EMS	Emergency Medical Services
EMT	Emergency Medical Technician (Basic, Intermediate, or Paramedic accredited).
EMTALA	Emergency Medical Treatment and Labor Act, the Federal "anti-dumping law" that ensures that emergency care is provided to anyone who needs it, regardless of their ability to pay or insurance coverage.
F	
Facility Recognition	Classification of a hospital emergency department where staff are specially trained to care for children, using appropriate pediatric equipment and following guidelines for age-appropriate medications
Family-Centered Care	An approach to health care that offers a new way of thinking about the relationships between families and health care providers (e.g., emotional, social, developmental support).
Federal Register	Government document announcing the availability and deadlines for applying for Federal grant programs.
FDA	Food and Drug Administration
First Responder	The initial level of care within an EMS system as defined by the EMS Education and Practice Blueprint, as opposed to a bystander.
FWA	Federalwide Assurance; an assurance of compliance with DHHS human subjects protection regulations
FY	Fiscal Year, a business year for an organization. For the Federal government and the EMSC NRC, it is October 1 through September 30. For CNMC, it is July 1 through June 30.
G	
GCP	Good clinical practice
Glasgow Coma Scale	This scale is used to quickly determine the status and degree of injury of a trauma victim to the head.
GLEMSCRN	Great Lakes EMSC Research Network
GMO	Grants Management Officer, the official responsible for the business management aspects of particular grants or cooperative agreements.
GPRA	Government Performance and Results Act
GME	Graduate Medical Education, the period of medical training that follows graduation from medical school; commonly referred to as internship, residency, and fellowship training.

Grant Guidance	Supporting documentation for Federal grant applications.
H	
Healthy People 2020	The prevention agenda for the nation. It is a statement of national opportunities – a tool that identifies the most significant preventable threats to health and focuses public and private sector efforts to address those threats
HEDA	Hospital Emergency Department Affiliate
HEDA PI	HEDA principal investigator; responsible for overseeing implementation of all PECARN studies at the HEDA
HIPPA	Health Insurance Portability and Accountability Act
HOMERUN	Hospitals of the Midwest Emergency Research Node
I	
I/O	Intraosseous Infusion, a medical procedure that can be used to bypass the veins and inject critical fluids directly into the bone marrow.
ICD-10	International Classification of Diseases, Tenth Edition, is the classification of diseases by diagnosis with four-digit numbers or alphanumeric descriptions. Used for billing purposes by hospitals and physicians.
ICH	International Conference on Harmonization; provides guidelines for conducting standardized research
ICU	Intensive Care Unit, having special medical facilities, services, and monitoring devices to meet the needs of gravely ill patients.
Institutionalization	The formal establishment of EMSC through the legislative or regulatory process, or by securing a private long-term funding commitment.
Interfacility transfer agreements	Written contracts between a referring facility (e.g., community hospital) and a specialized pediatric center or facility with a higher level of care and the appropriate resources to provide needed care required by the child. The agreements must formalize arrangements for consultation and transport of a pediatric patient to the higher-level care facility.
Interfacility guidelines	Hospital-to-hospital, including out of state/Territory, guidelines that outline procedural and administrative policies for transferring critically ill pediatric patients to facilities that provide specialized pediatric care.
Intubation	Insertion of an endotracheal tube to help an unconscious patient breathe.
IRB	Institutional Review Board
ISS	Injury Severity Score
M	
M&M	Morbidity/Mortality, is a conference held by many departments on cases that either ended in death (where there was an interesting diagnosis)--mortality, or someone with a good diagnosis -- morbidity.
Managed Care	Any form of health care plan that contracts selectively with providers, employers, or insurers to channel employees or patients to a specified set of cost-effective providers (a provider net-

	work). Providers implement procedures to ensure medically necessary and appropriate use of health care services.
MOO	Manual of Operations; provides detailed instructions for each study
MCH	Maternal and Child Health
Medicaid	A program of medical aid designed for those unable to afford regular medical service and financed jointly by the state and Federal governments.
Medical Control	Physician oversight of care provided by prehospital personnel. On-line medical control concerns real-time direction of prehospital providers by designated medical personnel. Off-line medical control relates to policies, training, and quality assurance.
Medical Home	A concept of medical care that ideally is accessible, continuous, comprehensive, family-centered, coordinated, and compassionate.
Medicare	A government program of medical care especially for the elderly.
Morbidity	A measure of disease incidence or prevalence in a given population, location, or other grouping of interest.
Mortality	A measure of deaths in a given population, location, or other grouping of interest.
MTDC	Modified total direct costs
MVC	Motor Vehicle Crashes
N	
NA	Nodal administrator; responsible for overseeing PECARN study implementation at nodal HEDAs
NEDARC	National EMS Data Analysis and Resource Center
Needs Assessment	Systematic appraisal of the type, depth, and scope of a problem.
NICU	Neo-natal Intensive Care Unit
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NM	Nodal manager; responsible for overseeing PECARN study implementation at nodal HEDAs
Nodal PI	Nodal principal investigator; responsible for nodal leadership
NRC:	National Resource Center (EMSC)
O	
Off-line Medical Direction	Treatment guidelines and protocols used by EMS providers to ensure the provision of appropriate pediatric patient care, available in written or electronic (e.g., laptop computer) form in the patient care unit or with a provider, at the scene of an emergency.
On-line Medical Direction	An individual is available 24/7 on the telephone, radio, or email to EMS providers who need on-line medical direction when transporting a pediatric patient to a hospital. The health professional (e.g., nurse, physician, physician assistant, EMT) providing medical direction is deemed to have pediatric expertise by the hospital in which they work and must have a higher level of pediatric training/expertise than the EMS provider to whom he/she is providing medical direction.

OHRP	Office of Human Research Protections
Outcome Evaluation	Used to obtain descriptive data on a project and to document short-term results.
Outcome Standards	Long-term objectives that define optimal, measurable future levels of health status, maximum acceptable levels of disease, injury, or dysfunction, or prevalence of risk factors.
Outcome	The consequence of a medical intervention on a patient.
Outcomes Research	Medical or health services research that attempts to identify the clinical outcomes (including mortality, morbidity, and functional status) of the delivery of health care.
P	
PALS	Pediatric Advanced Life Support, an educational program for health care providers (e.g., physicians, nurses, EMTs)
Patient Care Units	any vehicle owned by an entity responsible for 911 services (eg; hospital, fire department, law enforcement, community, etc.) that is licensed/regulated by the state/territory/county/local jurisdiction and is staffed by state/territory/county/local jurisdiction certified/licensed prehospital personnel whose primary responsibility is delivering emergency medical care to any and all patients in the out-of-hospital setting. This definition excludes any individual's personal vehicle(s).
PCC	Poison Control Center
PECARN	Pediatric Emergency Care Applied Research Network
PEM-NEWS	Pediatric Emergency Medicine Northeast, West & South
PEP	Pediatric Education for Prehospital Providers course.
Performance Measure	A specific measure of how well a health plan does in providing health services to its enrolled population. Can be used as a measure of quality.
PHI	Protected health information
PI	Principal Investigator, the individual designated by the recipient to direct the project or program being supported by the grant, and is responsible to recipient organization officials for the proper conduct of the project or program.
PICU	Pediatric Intensive Care Unit
Practice Guideline	An explicit statement of what is known and believed about the benefits, risks, and costs of particular courses of medical action, and intended to assist decisions by practitioners, patients, and others about appropriate health care for specific clinical conditions.
Prehospital	Time or care that occurs before or during transportation to a hospital. Part of the Continuum of Care.
Prevention	Actions taken to reduce susceptibility or exposure to health problems (primary prevention), detect and treat disease in early stages (secondary prevention), or alleviate the effects of disease and injury (tertiary prevention). Part of the Continuum of Care.
PRIDENET	Pittsburgh, Rhode Island, Delaware Network

Primary Care	A basic level of health care provided by the physician from whom an individual has an ongoing relationship and who knows the patient's medical history (e.g., preventive services, treatment of minor illnesses/injuries, identification of problems that require referral to specialists). Traditionally, primary care physicians are family physicians, internists, gynecologists and pediatricians.
PRIME	Pediatric Research in Injuries and Medical Emergencies
Process Evaluation	Examination of the procedures and tasks involved in implementing a program.
Program/Project Officer	An official who is responsible for the technical, scientific, or programmatic aspects of a grant, and works closely with the Grants Management Officer in the overall administration of grants.
Project Coordinator	The individual responsible for executing activities supported by the grant, and directed by the PI or Project Director.
Project Director	The individual designated by the recipient to direct the project or program being supported by the grant, and is responsible to recipient organization officials for the proper conduct of the project or program.
Protocols	Standardized guidelines for treatment procedures.
Public Health	Activities that society does collectively to assure the conditions in which people can be healthy. This includes organized community efforts to prevent, identify, preempt, and counter threats to the public's health.
Q	
Quality Assurance	A formal, systematic process to improve quality of care that includes monitoring quality, identifying inadequacies in delivery of care, and correcting those inadequacies.
R	
RC	Research coordinator
RCT	Randomized controlled trial
Registry	A repository for information that is used for data collection.
Regulation	A governmental order with the force of law.
Rehabilitation	The physical restoration of a sick or disabled person by therapeutic measures and reeducation to participation in the activities of a normal life within the limitations of the person's physical disability. Part of the Continuum of Care.
RFP	Request for Proposals, a funding announcement used by the Federal government to solicit proposals from applicants.
RNC	Research Node Center
S	
SAE	Severe adverse event; includes life threatening event or event that leads to disability or hospitalization
SCHIP	State's Child Health Insurance Program
Septic Shock	Septic shock is a serious medical condition caused by decreased tissue perfusion and oxygen delivery as a result of infection and sepsis. It can cause multiple organ failure and death. Its most common victims are children, immunocompromised individuals, and the elderly, as their

	immune systems cannot cope with the infection as well as healthy adults are able. The mortality rate from septic shock is approximately 50%.
SOPs	Standard operating procedures
Strategic Plan	A comprehensive, incorporating goals, objectives, activities, and evaluation.
Study Site PI	Principal investigator at a study site responsible for a specific PECARN study at the HEDA site
Surveillance	Observation of a particular issue to collect data.
T	
TBI	Traumatic Brain Injury
Technical Assistance	Provision of expert advice or guidance.
Telemedicine	The investigation, monitoring, and management of patients and the education of patients and staff using systems which allow ready access to expert advice and patient information, no matter where the patient or the relevant information is located.
Tertiary Care	Highly specialized health care usually over an extended period of time that involves advanced and complex procedures and treatments performed by medical specialists in state-of-the-art facilities.
Title V	Title V of the Social Security Act, which authorizes the MCH Block grant and other MCH programs.
Tracheostomy	The surgical formation of an opening into the trachea through the neck especially to allow the passage of air.
Trial DB	Trial Database; software used at the DCC for data collection for PECARN studies
Transport	The means by which ill or injured are transported to care (may be ground, air, or water).
Trauma	An injury caused by a physical force. Most often the consequences of motor vehicle crashes, falls, drowning, gun shots, fires and burns, stabbing, or blunt assault.
TRIPP	An encyclopedic resource guide that helps instructors teach ambulance personnel basic life-saving procedures for children.
Trust Funds	Accounts established by law to hold receipts collected by the federal government and earmarked for specific purposes and programs. These receipts are not available for the general purposes of the federal government.
W	
WBCARN	Washington, Boston, Chicago Applied Research Node
White Papers	Topic-specific papers developed by experts that generally provide recommendations for addressing a particular issue.
Work Plan	A plan of activities to be carried out to meet the scope of work approved in a grant or contract.


EMSC
Emergency Medical
Services for Children
NATIONAL RESOURCE CENTER


PECARN
Pediatric Emergency Care
Applied Research Network